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JULY, 1948

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This is a preliminary report on the surgical treatment of intractable asthma. While temporary dramatic relief has been obtained in severe cases of intractable asthma by unilateral left sided parasympathetic denervation and destruction of the pulmonary plexus, none of the cases in this series has been followed for a long enough period to predict the final outcome. Although final adoption of the surgical treatment of asthma must await extensive clinical and laboratory investigations, this report is published primarily to revive an interest in the subject.

The Surgical Treatment of Intractable Asthma

BRIAN BLADES*

THE GEORGE WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, WASHINGTON, D. C.

VARIOUS surgical procedures have been employed for bronchial asthma. Kummell¹ in 1923 operated upon the sympathetic nervous system for the treatment of asthma. Although he considered the vagus nerve supply as the chief motor innervation to the lung, he was fearful of the consequences of interfering with vagus fibers. Braeucker² who worked in Kummell's clinic had reported that stimulation of either the sympathetic or vagus systems might cause bronchial spasm. Accordingly, a unilateral cervical sympathectomy was performed in the hope that some of the motor fibers of the vagus entered the lung through the sympathetic system and would be destroyed. Kummell reported his original work with optimism, and interest was stimulated in the surgery of asthma throughout Europe.

Approximately a year after Kummell's original report, Kappis³ was equally optimistic concerning the results of vagotomy for asthma. He severed the vagus on the right side below

the level of the recurrent laryngeal nerve. Other surgeons have employed varying techniques for operations on both the sympathetic and parasympathetic nerves to the lungs in an effort to alleviate bronchial asthma. Leriche^{4,5} performed stellate ganglionectomy, and combined operations involving sympathectomy and unilateral vagotomy were employed by Kummell and others.

Although the sympathetic and parasympathetic systems have been the principal surgical targets, other organs have been altered or excised in attempts to cure asthma. For example, Freund⁶ in 1906 removed varying numbers of costal cartilages in patients with asthma and emphysema. The principle of this operation was to increase respiratory excursion. Hirschberg⁷ claimed to increase vital capacity of the emphysematous patient by transverse division of the sternum. Voelcher⁸ advocated both paravertebral thoracoplasty and exeresis of intercostal nerves.

In addition to surgical procedures involving the chest, operations on the nose and throat, thyroid and even the spleen⁹ are described in medical literature as beneficial in the treatment of intractable asthma.

*From the Department of Surgery, The George Washington University School of Medicine, Washington, D. C., and Walter Reed General Hospital, Washington, D. C.

Research Grant from Medical Research and Development Board, Surgeon General's Office, U. S. Army.



BRIAN BLADES

The scholarly paper of Phillips and Scott¹⁰ in 1929, on the surgical treatment of bronchial asthma, contains a review of the literature and a record of the various surgical procedures which have been tried and abandoned. They reported a case of intractable asthma in which the vagus nerve on the right was exposed, injected with novocaine, and the four main branches running to the posterior surface of the bronchi were divided. The main trunk of the vagus was freed and the nerve was cut at the inferior border of the right main bronchus. They state that sympathetic fibers were not identified but it seems likely that most of the sympathetic fibers involved in the posterior pulmonary plexus would have been destroyed. Their patient who considered life was unbearable before the operation, had absolute relief for three months. Even after exposure to horse dander to which he was extremely sensitive, he had only a mild attack of asthma and urged another patient to have the operation.

The next significant contribution to the sur-

gery of bronchial asthma was made by Rein-hoff and Gay¹¹⁻¹³ who in 1938 reported 11 cases of intractable asthma treated by bilateral posterior pulmonary plexus resections. Their approach to the problem resembles that of Kummell and Phillips and Scott and others who had operated upon the pulmonary plexus, except that bilateral intervention was routine. In 1942,¹³ a summary of their results revealed that of 21 patients treated by bilateral resection of the pulmonary plexus, 8 report striking beneficial results, 9 died as the result of the operation or later, and 4 showed no improvement.

MODERN contributions to the surgical treatment of asthma include the paper of Carr and Chandler¹⁴ on the role of dorsal sympathetic ganglionectomy for intractable asthma. Carr has made a careful and conservative evaluation of 5 patients treated by this method, observed from four to ten years. All of his 5 patients have gained weight and have been able to work. Only two of the group have been away from their occupations because of asthma for a year's period. All respond to small amounts of medication when an attack of asthma is impending. Osler Abbott discussed Carr's paper and stated that he has employed bilateral operations on the parasympathetic system for intractable asthma. It is particularly interesting that Abbott has considered the most beneficial results to be in patients with emphysema.

A review of past and current literature indicates that original surgical interventions were directed toward the sympathetic system principally because alterations of the parasympathetic chains were considered prohibitively dangerous. There is probably no question that the dangers of excising the pulmonary plexus and interference with vagus nerves exceed those of operations on the sympathetic system. Anatomic and experimental evidence, however, indicate strongly that extirpation of the pulmonary plexus is a better method to eliminate or reduce extrinsic nerve stimuli.

It appears that practically all preliminary re-

ports on the surgical treatment of bronchial asthma are characterized by initial enthusiasm. The diversiform nature of asthma makes any therapeutic measure a potential temporary success. A classic example of honest optimism is contained in a paper by Phillips,¹⁵ published in 1818, who reported that the simple application of galvanic current to the chest produced 20 or 30 cures of asthma.

Available data on the surgical treatment of asthma are insufficient to warrant conclusions concerning the future of justifiable surgical interventions for relief of this disease. It seems likely that early attempts may have been abandoned because of distressingly high operative mortality. Refinements in operative technics, and, more important, improvements in anesthesia should reduce greatly the immediate risks of operation. In this connection, it is interesting that nitrous oxide and cyclopropane have been employed as anesthetic agents for patients with asthma in the past. This is surprising since ether and avertin act as bronchial dilators and both experimental and clinical evidence indicate their use.

Another difficulty which has undoubtedly interfered with the study of asthma has been an inability to produce controlled bronchial spasm in experimental animals. Efforts in our own laboratory with histamine-produced bronchial spasm has not been applicable to the clinical problems.

There are several valid reasons to reinvestigate the possibilities of the surgical treatment of asthma. Most of the work on the subject was done during a period when simple exploration of the chest involved serious risks. The dramatic developments in the field of anesthesiology have greatly reduced these dangers. Even during the time when surgeons were handicapped by lack of both experience and equipment for working in the open chest, some gratifying results were reported. This may justify further endeavors in suitable cases, and finally the realization that certain cases in the field of psychosomatic medicine will require surgical rearrangement of the nervous system.

This preliminary report will not include a

discussion of the various types of asthma. Whether extrinsic or intrinsic disease should have a bearing on a decision to recommend surgical treatment is apparently unknown. Warnings of the psychogenic factor appear often in the literature of the past. Precise evaluation is again impossible.

CASE REPORTS

Case 1—The patient, a 29-year-old white female was first seen in June 1947 at Walter Reed General Hospital. She was receiving oxygen and helium and appeared to be in a moribund condition. Adrenalin, aminophylline, morphine, and benadryl had been employed without benefit. Ether in oil and avertin were tried with no appreciable effect on the status asthmaticus and finally intravenous ether (50 cc. of ether in 1,000 cc. of saline, 100 mg. per kilogram of body weight) was employed. Some relief was obtained and the patient regained consciousness. Asthmatic wheezing continued but enough respiratory exchange was maintained to relieve cyanosis.

This patient had had bronchial asthma for fifteen years. For the past four years she was unable to live at home and was hospitalized on many occasions. During this four-year period she had 13 episodes of status asthmaticus severe enough to cause unconsciousness.

She was completely "adrenalin fast"; no benefit from the drug in controlling the disease had been noted for two years.

Complete and careful studies had been made concerning sensitivity to various agents. She was allergic to many things but particularly to house dust and cabbage. Attempts at desensitization had failed.

THE situation was so desperate that surgical intervention was considered. Failure of sympathetic nerve blocks in other patients and perhaps the fact that adrenalin had no effect on this case resulted in the decision to alter the parasympathetic nervous system. For reasons unknown, the majority of recorded unilateral

operations on the vagus for asthma have been on the right side. On the basis that the arterial side of the chest might have a more abundant parasympathetic nerve supply, a left-sided approach was employed.

It is important to record that the patient was informed that the chance of success was small and that probably a second operation on the right side would be necessary.

Under avertin-ether anesthesia, a left posterolateral incision was made over the fifth rib. After division of the overlying muscles, a long segment of the fifth rib was resected subperiosteally. The pleura was incised and the left thoracic cavity exposed by means of rib-spreading retractors.

Alterations of the nerve supply consisted of the following steps: (1) identification of the left vagus nerve at the level of the pulmonary plexus; (2) the vagus was freed and retracted gently, but not cut; (3) the pulmonary plexus was destroyed; (4) all visible branches of the vagus to the pulmonary hilum and lung were divided; (5) esophageal branches and the main trunk of the vagus were preserved (esophageal branches become evident at about the level of the inferior pulmonary vein); (6) the sheaths of the great vessels, e.g., pulmonary artery and veins, were cleaned away as much as possible; (7) the pulmonary ligament was divided in order to destroy any fibers entering through it.

The chest wall was reconstructed in layers and the thorax closed without drainage after the lung was fully re-expanded.

During the first two weeks after the operation audible wheezes could be heard in the right lung. These were not evident on the left, but it is my opinion that this alteration of physical signs on the left resulted from the effects of an open thoracotomy and are therefore of no significance.

The patient's subsequent progress has been dramatic. She has had no attacks of asthma, does her own house work, eats cabbage, which she relishes, in great quantity and has gained 25 pounds. She has cooperated in trying to provoke attacks of asthma, particularly in connec-

tion with diet (cabbage) and contacts with house dust.

Case 2—A 37-year-old Negro male was admitted to the George Washington University Surgery Section of Gallinger Hospital. The patient had had asthma all his life. He moved from Georgia to the District of Columbia, hoping to find relief. This proved a vain hope.

Since 1937, it was unusual for him to have a day without wheezing and tightness in the chest. There was no seasonal distribution or specific allergen to be identified.

HOSPITALIZATION was required on approximately 20 occasions with a diagnosis of asthma and pneumonia. He had been given benadryl daily for about one year. Adrenalin had little effect on the attacks.

There is an additional and important feature in this case, namely, advanced emphysema associated with the asthma, and, in the opinion of Doctor Benjamin Manchester, cardiologist on the George Washington University Medical School Staff, *cor pulmonalis*.

An operation identical to that described in Case 1 was performed in July 1947. Shortly after induction of anesthesia, the patient stopped breathing spontaneously and it was necessary for the anesthesiologist, Doctor Lloyd H. Mousel, to maintain respiratory exchange for about four hours. Spontaneous respirations did not recur until approximately one hour after the operation was completed.

Emphysema of the left lung was so marked that the organ showed no sign of collapse when the thorax was opened. It is obvious that a combination of intractable asthma, emphysema, and *cor pulmonalis* made this subject a poor operative risk.

His condition remained serious for the first four postoperative days. It was not necessary, however, to give any medication for attacks of asthma. Following this critical period his condition improved rapidly and since July 1947 he has had no attacks of asthma, feels well, and enjoys full activity. Complete studies of the cardiac status before and after operation indi-

cate to Doctor Manchester that there has been marked improvement.

CASES 3 and 4 will not be discussed in detail. One patient, a young woman with intractable asthma of four years' duration, who for a year has received aminophylline almost daily, believes she has obtained beneficial results. As is the case with the other patients, postoperative observation has not been long enough to determine the final result.

Case 4 is of interest because of the peculiar but perhaps significant complicating factors. The patient, who is an inmate of St. Elizabeth's Hospital, has been under observation for an extended period with a diagnosis of schizophrenia. Since all students of asthma are interested in the role of psychogenic factors, this particular subject is, therefore, of significance.

This patient, a 35-year-old Negro, while under treatment for the psychiatric condition, had required almost daily medication for asthma

since August 1947. After unilateral parasympathetic denervation and destruction of the pulmonary plexus, he has been free of symptoms and requires no medication.

SUMMARY

1. A preliminary report on the surgical treatment of intractable asthma is presented in the hope of reviving interest in the subject.

2. Surgical intervention should not be considered until conservative measures have failed completely.

3. All of the cases in this series have been followed for too short a period to predict the final outcome.

4. Temporary dramatic relief has been obtained in severe cases of intractable asthma by unilateral, left sided parasympathetic denervation and destruction of the pulmonary plexus.

5. Final adoption of the surgical treatment of asthma must await extensive clinical and laboratory investigations.

REFERENCES

1. KUMMELL, H., SR.: Die operative Heilung des Asthma bronchiale. *Klin. Wchnschr.* 2:1825, 1923.
2. BRAUCKER, W.: Die experimentelle Erzeugung des bronchial Asthmas und seine operative Beseitigung (Anatomisch-Chirurgische Studie). *Arch. f. klin. Chir.* 137:463, 1925.
3. KAPPEL, M.: Die Frage der operativen Behandlung des Asthma bronchiale. *Med. Klin.* 20:1347, 1924.
4. LERICHE, R., and FONTAINE, R.: Resultats éloignes der traitement chirurgical de l'asthma bronchique. *Bull. et mém. Soc. nat. de chir.* 54:6600, 1928.
5. LERICHE, R., and FONTAINE, R.: Position actuelle de la question die traitement chirurgical de l'asthme bronchique. *Arch. méd.—chir. de l'app. respir.* 4:1, 1928.
6. FREUND, W. A.: Zur operativen Behandlung Gewisser Lungen Kran Kherten, Bernhenden aveolaren Emphysems (mit einem Operationsfalle). *Ztschr. f. exper. Path. u. Therap.* 3:379, 1906.
7. HIRCHBERG: Quoted by PHILLIPS and SCOTT.¹⁰
8. VOELCHER: Behandlung des Asthma bronchiale durch paravertebale Feilerresektion. *Arch. f. klin. Chir.* 148:52, 1927.
9. HYNFK, K.: Asthma and splenectomy. *Bratisl. lekár. listy.* 7:218, 1927.
10. PHILLIPS, E. W., and SCOTT, W. J. M.: The surgical treatment of bronchial asthma. *Arch. Surg.* 19:1425, 1929.
11. RIENHOFF, W. M., and GAY, L. N.: *Arch. Surg.* 37:456, 1938.
12. GAY, L. N., and RIENHOFF, W. M.: *Bull. Johns Hopkins Hosp.* 70:386, 1942.
13. GAY, L. N., and RIENHOFF, W. M.: *J. Allergy* 13:626, 1942.
14. CARR, DUANE, and CHANDLER: High dorsal sympathetic ganglionectomy for intractable asthma. *J. Thoracic Surg.* 17:1, 1948.
15. PHILLIP, A. P. N.: An experimental enquiry into the laws of the vital function. Philadelphia, 1818.

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Results of insulin tests on 2 were negative and no insulin test had been done on the third. Roentgenographic studies on one did not give any evidence of ulceration and postoperative roentgenologic examinations were not made on the other 2.

The proved incidence of recurring ulceration, therefore, is 6 per cent in the 50 cases in which one of us (W. W.) carried out resection of the vagus nerves in the period from March 1946, to March 1, 1947, and symptoms of ulcer persisted in another 6 per cent.

The question has been raised whether the technic of the transabdominal resection of vagus nerves, which was used in these cases and in others which we have reported, has resulted in complete vagotomy. The answer is: If the Hollander insulin test is an indication of the completeness with which the vagus nerves in the stomach are resected, then complete vagotomy was accomplished in all 3 cases of proved recurring ulceration and in 2 of the 3 cases in which the symptoms of ulcer persisted, for in all 5 cases, results of insulin tests were negative. Moreover, the exposure of the lower part of the esophagus and the vagus nerves, which was obtained during the course of the operation of transabdominal resection of the vagus nerves, was good as was indicated by the motion picture which followed this presentation at the meeting.

UNFORTUNATELY recurring ulceration is not the only serious complication which follows the operation, for in studying the effects of the operation on the motility of the gastrointestinal tract, nine months after operation, we have found that 12 per cent of the patients have had persistent, troublesome symptoms, such as bloating, belching of foul-smelling gas, loss of appetite, and sometimes vomiting or diarrhea, a series of complications which have been most difficult to control. Some of these patients have complained bitterly of these symptoms. It was our hope that administration of urethane of beta-methylcholine chloride (urecholine) as a parasympathetic stimulant would



WALTMAN WALTERS

be helpful in relieving the discomfort since Ruffin, Grimson, and Smith³ have shown that it will increase the frequency and amplitude of waves of gastric peristalsis. Recently 4 of our patients who have severe early postoperative disturbance of motility received no benefit from the use of urethane of beta-methylcholine chloride. In all, results of insulin tests were negative. Our experience with this preparation in relieving the distress of the vagotomized atonic stomach has been disappointing.

That the operation is not without an immediate and possibly a future risk cannot be denied even though that risk is small. In one of our colleagues' cases in which resection of the vagus nerves and posterior gastroenterostomy were performed simultaneously in the treatment of a duodenal ulcer, persistent gastric retention with hypoproteinemia occurred. In spite of all efforts directed toward control of these factors the patient died on the fourteenth day after operation. At necropsy an unsuspected subdiaphragmatic abscess, the result

Favorable and Unfavorable Results of Resection of the Vagus Nerves for Peptic Ulcer

WALTMAN WALTERS¹ AND HAROLD A. NEIBLING²

MAYO CLINIC AND MAYO FOUNDATION, ROCHESTER

LAST YEAR in speaking before the meeting of the Interstate Postgraduate Medical Association one of us (W. W.) considered some of the recent advances in the management of surgical lesions of the upper part of the abdomen.¹ At that time also rather brief reference was made to experience with resection of the vagus nerves or vagotomy in 21 cases of peptic ulceration. Operations in these 21 cases had been performed in the preceding eight months. In one of these cases a large recurring perforating gastric ulcer had developed after complete vagotomy and had produced symptoms which necessitated its removal by partial gastrectomy (Case 1, Table 1).

UNFAVORABLE RESULTS

Since that time recurring perforating craterous peptic ulcers have followed complete vagotomy or resection of the vagus nerves in 2 additional cases in our series (Cases 2 and 3, Table 1). This operation was performed in association with anterior gastroenterostomy and

jejunojejunostomy in one case and with excision of the gastrojejunal ulcer, disconnection of the gastroenteric anastomosis, and pyloroplasty in the other. In the former case pain necessitated a second operation on August 15, 1947. A recurring anastomotic ulcer perforating into the abdominal wall was found and partial gastrectomy was carried out. The other patient who underwent resection of the vagus nerves on October 14, 1946, returned at our request for re-examination on August 24, 1947, at which time there was roentgenographic evidence of a recurring perforating duodenal ulcer with crater. The insulin test on August 26, 1947, gave negative results. In both of these cases the results of the Hollander² insulin tests were negative which, according to Dragstedt, is indicative of complete severance of the vagus nerves of the stomach.

In another case roentgenographic evidence of jejunitis was found four weeks subsequent to operation. This patient, however, did not have any recurrence of the ulcer symptoms which were severe before operation. The insulin test on this patient, likewise, gave negative results.

Three additional patients in our series (Table 2) continued to have distress of ulcer type for nine to ten months following their operations.

¹Division of Surgery, Mayo Clinic, Rochester, Minnesota.

²Fellow in Surgery, Mayo Foundation, Rochester, Minnesota.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

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That the operation is not without an immediate and possibly a future risk cannot be denied even though that risk is small. In one of our colleagues' cases in which resection of the vagus nerves and posterior gastroenterostomy were performed simultaneously in the treatment of a duodenal ulcer, persistent gastric retention with hypoproteinemia occurred. In spite of all efforts directed toward control of these factors the patient died on the fourteenth day after operation. At necropsy an unsuspected subdiaphragmatic abscess, the result

of perforation of the duodenal ulcer, was found. Resection of the vagus nerves apparently masked the symptoms of perforation in this case and may have done so in 2 of our cases in which recurring ulcers developed. In one of these cases pain occurred in the lower anterior portion of the thorax and the left upper part of the abdomen on motion, which probably was the result of the perforation of the gastrojejunal ulcer with its base on the abdominal wall. Moreover, in this case relief of distress by food and soda was not the same as that frequently noted in the presence of perforating gastrojejunal ulcer when vagotomy had not been performed. The other patient has had no pain typical of ulcer but has lost his appetite during the past three months (seven months after vagotomy, disconnection of the gastroenteric anastomosis, excision of a gastrojejunal ulcer, and pyloroplasty). The roentgenogram shows a recurring duodenal ulcer with a crater.

In speculating on causes of relief of pain referable to the ulcer immediately following vagotomy, we have called attention previously to the fact that the relief of pain was not due to the healing of the ulcer, first, because it could not heal in such a short time but also because, in 4 of our cases in which pain was relieved, roentgenographic examination from two and a half to three weeks after operation revealed persistence of the peptic ulceration.

During the first three months' period (March, April, and May 1946) in which one of us (W. W.) was performing transabdominal vagotomy, we were a little reluctant to accept the risk incurred in reducing the patient's blood sugar level to 40 mg. per 100 cc. or less by injections of insulin in order to determine whether the volume of gastric acids would increase. If increase occurs, the result of the test is considered positive and a positive reaction indicates that all of the branches of the vagus nerves to the stomach had not been cut. After the problem was discussed with one of our surgical friends from another clinic, who assured us that he had carried out the procedure in many cases without risk, we began using it as a routine procedure approximately ten to

fourteen days after vagotomy if the patient's general condition permitted. Therefore, from that time on we have obtained insulin tests in 39 out of 40 cases. A study of these insulin tests discloses that in 67 per cent of the cases negative results were obtained. These negative results indicate that all branches of the vagus nerves to the stomach had been resected. In 33 per cent of the 40 cases, however, the tests gave positive results. In both groups we have studied the response to resection of the vagus nerves alone and in combination with other operations on the stomach with regard to (1) relief of symptoms of ulcer, (2) reduction of gastric acidity, and (3) the incidence of motility disturbances producing troublesome symptoms.

In the cases in which results of the insulin tests were positive, a greater reduction of gastric acidity occurred and achlorhydria developed in a greater percentage than in the cases in which insulin tests were negative. These figures were 93 per cent and 69 per cent, respectively. The incidence of troublesome disturbances of motility were about equal in the two groups. The most striking observation, however, is the fact that nearly all recurrences of ulceration took place in the group of cases in which the results of insulin tests were negative, a circumstance which we are unable to explain.

IN TRYING to explain the difference in these results with those reported by Dragstedt⁴ and his associates, we have compared the relative incidence in which the operation was performed for duodenal ulcer, gastrojejunal ulcer, and gastric ulcer by ourselves, by Ruffin, Grimson, and Smith³ from Duke University, by Moore and his associates⁵ from the Massachusetts General Hospital, and by Colp⁶ from Mount Sinai Hospital, New York. Eighty-six per cent of Dragstedt's patients had duodenal ulcer and 9 per cent had gastrojejunal ulcer. In our series, 68 per cent (34 patients) had duodenal ulcer and 14 per cent had gastrojejunal ulcer. If the 68 cases in which operations on the vagus nerves were performed by other surgeons at the Mayo Clinic are added, the percentages are

TABLE I
DEFINITE RECURRENCE OF ULCER AFTER VAGOTOMY

CASE	ULCER AND TIME OF VAGOTOMY	ASSOCIATED OPERATION	RESULT OF INSULIN TEST	POSTOPERATIVE SYMPTOMS	POSTOPERATIVE ROENTGENOLOGIC DIAGNOSIS AND DATE	TREATMENT
1	Gastric ulcer 7-29-46	Excision of ulcer	Negative	Ulcer distress	Penetrating gastric ulcer 12-18-46	Medical management unsuccessful; high gastric resection 1-13-47 for penetrating gastric ulcer
2	Duodenal ulcer 8-26-46	Anterior gastroenterostomy with subsequent jejuno-jejunostomy	Negative	Atypical ulcer distress	Negative; gastroscopic positive for ulcer 8-1-47	Take down gastroenteric stoma; resection of stomach 8-15-47 for anterior penetrating gastrojejunal ulcer
3	Gastrojejunal ulcer 10-14-46	Removal of gastroenteric stoma, excision of ulcer and pyloroplasty	Negative	Poor appetite; moderate distress	Duodenal ulcer with crater 8-27-47	Medical management

65 for duodenal ulcer and 29 for gastrojejunal ulcer. It is interesting to note that the percentage of patients operated on for duodenal ulcer and gastrojejunal ulcer reported by the others referred to, except Dragstedt, practically parallel those of the Mayo Clinic series (Table 3).

Resection of the vagus nerves without associated operation on the stomach was done in only 17 of our 50 cases and in 31 of the 68 cases of our colleagues at the clinic. In 10 cases of our group the operation was performed for duodenal ulcer. The reason for the small number of cases of duodenal ulcer in which this operation alone was carried out was that in the other cases of duodenal ulcer the ulcer was so large and seemed to be of such an obstructive or potentially obstructive nature that some type of drainage operation of the stomach, such as gastroenterostomy, and in a few cases, gastric resection was thought advisable and in cases of gastrojejunal ulcer it was considered worth while in most cases to remove the gastrojejunal ulcer and disconnect the gastroenteric anastomosis at the time of vagotomy. In 2 cases the gastrojejunal ulcer was not removed and the gastroenteric anastomosis was not disconnected.

In 87 per cent of the cases of duodenal ulcer at the Mayo Clinic medical treatment has been

employed in recent years. In the complicated cases of duodenal ulcer in which operation has been performed, partial gastrectomy with partial duodenectomy has been the operation of choice. Resection of the vagus nerves has been performed in some cases of this type, in cases of gastrojejunal ulcer, and gastric ulcer.

IF RESECTION of the vagus nerves were employed in more duodenal ulcer cases in which the lesion is now treated medically, results of this operation might be expected to be better than they have proved in our series.

Small*,⁷ one of my assistants, has made an intensive review of the literature relating to the effects of vagotomy in animals and the clinical results of patients with peptic ulceration. Time does not permit more than the briefest reference to these historical data. However, neither those working on the problem experimentally nor those working on it clinically to the time Dragstedt's contribution was made were able to demonstrate to Small's satisfaction that a decisive viewpoint could be reached regarding results of the procedure in animals or patients.

One of the interesting contributions, in our

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of perforation of the duodenal ulcer, was found. Resection of the vagus nerves apparently masked the symptoms of perforation in this case and may have done so in 2 of our cases in which recurring ulcers developed. In one of these cases pain occurred in the lower anterior portion of the thorax and the left upper part of the abdomen on motion, which probably was the result of the perforation of the gastrojejunal ulcer with its base on the abdominal wall. Moreover, in this case relief of distress by food and soda was not the same as that frequently noted in the presence of perforating gastrojejunal ulcer when vagotomy had not been performed. The other patient has had no pain typical of ulcer but has lost his appetite during the past three months (seven months after vagotomy, disconnection of the gastroenteric anastomosis, excision of a gastrojejunal ulcer, and pyloroplasty). The roentgenogram shows a recurring duodenal ulcer with a crater.

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tion is performed without vagotomy. Although relief of ulcer distress occurred in 22 of our 24 cases, recurring ulceration necessitated gastric resection in 1 and troublesome disturbances of motility were present for at least nine months in 6 cases.

Resection of the vagus nerves has no place in the treatment of chronic gastric ulcer if the ulcer can be removed in the course of partial gastrectomy. In 9 of our 50 cases resection of the vagus nerves was done for gastric ulcer. Recurrence of ulcer took place in 1 case and disturbances of gastric motility persisted for seven months or longer in 3.

Experience and time will be required to tell just what place resection of the vagus nerves has in the treatment of duodenal and gastrojejunal ulceration.

In 1946, resection of the stomach for gastric ulcer was performed in 101 cases with a mortality rate of 2.0 per cent. In the same year gastric resection for duodenal ulcer was done in 296 cases with a mortality rate of 2.0 per cent. In view of the low mortality rate and good results in these cases, resection of the stomach and not resection of the vagus nerves seems on the whole to be the operation of choice for both duodenal and gastric ulcers.

SUMMARY OF RESULTS IN OUR SERIES

Resection of vagus nerves alone—In our series of 50 cases to date vagotomy alone was done without other procedure in 10 for duodenal ulcer, in 2 for gastrojejunal ulcer, and in 5 for gastric ulcer. All of the patients obtained relief of the pain caused by ulcer. In 3 cases of duodenal ulcer and in 1 of gastric ulcer disturbances of motility occurred after vagotomy. In one case of duodenal ulcer and one of gastric ulcer the results of one insulin test in each case after operation were positive and in neither case was gastric acidity reduced. Four of the patients with duodenal ulcer were reported at dismissal (approximately two and a half to three weeks after operation) as still having visible ulcers on roentgenologic examination. Two of these patients gave a positive reaction

to the insulin test.

Resection of vagus nerves and other gastric operations—Vagotomy with a simultaneous gastric operation was performed in 24 cases of duodenal ulcer, in 5 of gastrojejunal ulcer, and in 4 of gastric ulcer. In 22 of the 24 cases of duodenal ulcer, in 4 of the 5 cases of gastrojejunal ulcer, and in 2 of the 4 cases of gastric ulcer, relief of distress from the ulcer was obtained. Ulceration recurred in one case of gastric ulcer and in one case of duodenal ulcer and subtotal gastrectomy was necessary six and ten months later. The gastric ulcer failed to heal in another case, and in one case a duodenal ulcer recurred after excision of a gastrojejunal ulcer. In all, gastric acidity was reduced and reactions to the insulin test after vagotomy were negative. In 6 cases of duodenal ulcer for which vagotomy and associated gastroenterostomy were carried out, in 2 cases of gastrojejunal ulcer, and in 3 cases of gastric ulcer, moderate to marked disturbances of motility developed. Of these, one of the patients with duodenal ulcer who reacted negatively to the insulin test and one patient with gastrojejunal ulcer who reacted positively to the insulin test had no reduction in gastric acidity after operation.

REFERENCES

1. WALTERS, WALTERMAN: Developments in surgery of the upper abdomen. *Postgrad. Med.* 1:360 (May) 1947.
2. HOLLANDER, FRANKLIN: Discussion. *Gastroenterology* 3:466 (December) 1944.
3. RUFEN, J. M., GRIMSON, K. S., and SMITH, R. C.: The effect of thoracoscopic vagotomy upon the clinical course of patients with peptic ulcer. *Gastroenterology* 7:599 (December) 1946.
4. DRAGSTEDT, L. R.: Section of the vagus nerves to the stomach in the treatment of gastro-duodenal ulcer. *Minnesota Med.* 29:597 (June) 1946.
5. MOORE, F. D., CHAPMAN, W. P., SCHULZ, M. D., and JONES, C. M.: Transdiaphragmatic resection of the vagus nerves for peptic ulcer. *New England J. Med.* 234:241 (February 21) 1946.
6. COLP, RALPH: Discussion. *Proc. Staff Meet., Mayo Clin.* 22:288 (July 23) 1947.
7. SMALL, J. T.: Denervation of the stomach: historical review. *Arch. Surg.* 55:189 (August) 1947.
8. HARTZELL, J. B.: The effect of section of the vagus nerves on gastric acidity. *Am. J. Physiol.* 91:161-171 (December) 1929.
9. VANZANT, F. R.: Late effects of section of the vagus nerves on gastric acidity. *Am. J. Physiol.* 99:375-378 (January) 1932.
10. PRIESTLEY, J. T.: The surgical treatment of jejunal ulcer. *Pennsylvania M. J.* (In press.)

TABLE 2

SUSPECTED RECURRENCES OF ULCER NOT CONFIRMED
BY ROENTGENOLOGIC EXAMINATION

CASE	TYPE OF ULCER AND DATE OF VAGOTOMY	ASSOCIATED OPERATION	RESULT OF INSULIN TEST	POSTOPERATIVE SYMPTOMS
4	Duodenal ulcer 10-31-46	Posterior gastro- enterostomy	Negative	Ulcer distress; fullness; vomit- ing; loss of weight
5	Gastric ulcer and gastritis 9-27-46	Gastrotomy	Negative	Ulcer distress gradually diminishing; occasional vomiting
6	Duodenal ulcer 6-6-46	Anterior gastro- enterostomy	None	Ulcer distress

opinion, indicating that results of vagotomy might be transitory, was that of Hartzell⁸ and Vanzant⁹ who showed that from six months to two years after resection of the vagus nerves of the stomach of dogs, gastric acidity and motility returned to normal. The recent clinical reports of Moore and associates indicate that the same recur in some human beings.

INDICATIONS FOR RESECTION OF THE VAGUS NERVES

The greatest field of usefulness for resection of the vagus nerves seems to be in the treatment of ulceration after partial gastrectomy. Recently Priestley¹⁰ has reported on a collected series of 16 cases of ulceration after partial gastrectomy for which vagotomy was performed at the Mayo Clinic. Results were good in 12, fair in 3, and poor in 1 case. In the same study in 21 cases of gastrojejunal ulcer after gastroenterostomy good results have followed resection of the vagus nerves in 19 cases, fair results in 2 and poor results in none. Despite these figures we are inclined to look with skepticism at this time on the chance that healing of all gastrojejunal ulcers developing after gastroenterostomy will result from resection of the vagus nerves alone. The reason for this skept-

TABLE 3

COMPARATIVE STATISTICS OF REPORTED VAGOTOMIES

	CASES	DUODENAL ULCER		GASTRO- JEJUNAL ULCER		GASTRIC ULCER	
		CASES	PER CENT	CASES	PER CENT	CASES	PER CENT
Dragstedt	170	147	86	15	9	8	5
Mayo Clinic Our series	50	34	68	7	14	9	18
Total series	118	77	65	34	29	7	6
Grimson	57	40	70	10	18	7	12
Moore	74	57	77	16	22	1	1
Colp	33	20	61	12	36	1	3

icism is a case which we have mentioned previously. In this case a perforating gastrojejunal ulcer developed and required partial gastrectomy approximately ten months after anterior gastroenterostomy, resection of the vagus nerves, and subsequent jejunojejunostomy (Table 1). The result of the insulin test was negative in this case.

RESECTION of the vagus nerves has so far seemed to have merit in cases in which dyspepsia caused by chronic duodenal ulcer does not respond to a medical regimen and the duodenal ulcer at operation is found to be small and not obstructive and other operations are not necessary on the stomach. In the 10 cases of our series in which this type of lesion was present resection of the vagus nerves has relieved the pain of ulcer at the expense, however, of dilation of the stomach with troublesome symptoms of disturbances of motility in 3. When resection of the vagus nerves was combined with other operations, such as gastroenterostomy, as it was in 24 cases of duodenal ulcer in our series, no improvement in the results is evident over those which experience of many years in many cases has shown occurs when gastroenterostomy or some other opera-

tion is performed without vagotomy. Although relief of ulcer distress occurred in 22 of our 24 cases, recurring ulceration necessitated gastric resection in 1 and troublesome disturbances of motility were present for at least nine months in 6 cases.

Resection of the vagus nerves has no place in the treatment of chronic gastric ulcer if the ulcer can be removed in the course of partial gastrectomy. In 9 of our 50 cases resection of the vagus nerves was done for gastric ulcer. Recurrence of ulcer took place in 1 case and disturbances of gastric motility persisted for seven months or longer in 3.

Experience and time will be required to tell just what place resection of the vagus nerves has in the treatment of duodenal and gastrojejunal ulceration.

In 1946, resection of the stomach for gastric ulcer was performed in 101 cases with a mortality rate of 2.0 per cent. In the same year gastric resection for duodenal ulcer was done in 296 cases with a mortality rate of 2.0 per cent. In view of the low mortality rate and good results in these cases, resection of the stomach and not resection of the vagus nerves seems on the whole to be the operation of choice for both duodenal and gastric ulcers.

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REFERENCES

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3. RUTIN, J. M., GRIMSON, K. S., and SMITH, R. C.: The effect of transthoracic vagotomy upon the clinical course of patients with peptic ulcer. *Gastroenterology* 7:599 (December) 1946.
4. DRAGSTEDT, L. R.: Section of the vagus nerves to the stomach in the treatment of gastro-duodenal ulcer. *Minnesota Med.* 29:597 (June) 1946.
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8. HARTZELL, J. B.: The effect of section of the vagus nerves on gastric acidity. *Am. J. Physiol.* 91:161-171 (December) 1929.
9. VANZANT, F. R.: Late effects of section of the vagus nerves on gastric acidity. *Am. J. Physiol.* 99:375-378 (January) 1932.
10. PRIESTLEY, J. T.: The surgical treatment of jejunal ulcer. *Pennsylvania M. J.* (In press.)

Recent Laboratory Methods and Their Interpretation

R. B. H. GRADWOHL*

ST. LOUIS

THE diagnosis of disease has been notably assisted in the last quarter of a century by remarkable developments in laboratory methods. The purpose of this discussion is to point out some of the outstanding advances.

The diagnosis of early carcinoma is one of the most important advances. It is carried out by examination of vaginal smears to pick up early cases of carcinoma of the uterus, by the study of malignant cells in sputum and bronchial secretions in the diagnosis of bronchogenic carcinoma, and by the examination of centrifuged urinary sediment in the diagnosis of malignant lesions of the urinary tract. This means of diagnosis is primarily based on the epic-making work of Papanicolaou and Traut. Many other workers have since followed their first steps.

The diagnosis of uterine carcinoma, utilizing these methods, has materially advanced; these methods are also applicable to large-scale operations or screening. In other words, if these methods are applied to vaginal secretions of every woman in a large clinical service, a number of cases will be picked up before clinical

symptoms or biopsy results would have proved the condition. These methods as applied to vaginal smears are by no means intended to supplant biopsy technic, but are used as an adjunct to it.

The staining procedure consists of fixing smears in a mixture of equal parts of 95 per cent alcohol and ether for five to fifteen minutes. When slides are to be sent to a hospital laboratory for staining, a drop or two of glycerin between two fixed slides provides very adequate protection for shipment. Rinse successively in 70 and 50 per cent alcohol and distilled water and then stain in Harris hematoxylin for two to six minutes. Decolorize by rapid immersion into a 0.5 per cent aqueous hydrochloric acid solution. The intensity of the color depends on how many times the slide is immersed in alcohol. Depth of color must be checked microscopically. The slide is placed in running water for five minutes and finally rinsed in distilled water. The preparation is then passed successively through 50, 70, 80, and 95 per cent alcohol. For rapid preparation a single 70 per cent alcohol bath may replace the above graded series. The slide is now stained for one minute in OG-6, which is a single Orange G stain. The counter-stained slide is now rinsed five to ten times in each of

*Director, Gradwohl School of Laboratory and X-ray Technique, St. Louis.

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two jars containing 95 per cent alcohol. It is then placed in EA-50 for two minutes. EA-50 is a multiple polychrome stain.* Rinse the preparation five to ten times in each of three jars containing fresh 95 per cent alcohol. Transfer to absolute alcohol and xylol and mount in clarite, Canada balsam, or gum dammar.

In order to attain proficiency in this method of diagnosis, pathologists must learn the normal appearance of vaginal smears by studying the various cells associated with hyperplasia, endometritis, and normal postpartum. They must learn to recognize carcinomatous cells from cervix and endometrium. In other words, it requires a thorough study of cytology to become proficient in evaluating the findings.

In addition to uterine carcinoma, splendid work has been done in the detection of bronchogenic carcinoma by microscopic examination of sputum and bronchial secretions. The work of Woolner and McDonald of the Mayo Clinic is notable in this regard. Their technic differs slightly from that of Papanicolaou. These workers found malignant cells in the sputum or in bronchial secretions where tumors involved the hilar regions. Whether or not typical cells can be found in sputum depends on whether a direct connection can be traced between the tumor and the main bronchial tree. It is necessary to recognize the normal epithelial cells found in this material, including squamous cells which line the mouth and pharynx and ciliated columnar cells which line the trachea and bronchi. They divide these bronchogenic carcinomas into three groups: (1) undifferentiated or anaplastic carcinoma, (2) squamous cell carcinoma, and (3) adenocarcinoma.

ANOTHER important advance in the diagnosis of malignancy is by means of microscopic examination of urinary sediment. This has been covered by another contribution from the Mayo Clinic, namely, the work of Daut and McDonald. Their method consists of collecting



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the urine in 95 per cent alcohol, centrifuging, decanting, and placing a drop of the sediment on a slide with a pipette, drying the smear, and staining with Papanicolaou's staining methods. Also, sediment may be stained with methylene blue and fat may be stained with Sudan IV.

Cytologic diagnosis of malignant processes, according to these workers, is based on (1) the nucleus (size, anisonucleosis, poikilonucleosis, hyperchromatosis, fragmentation, multiplicity); (2) the nucleolus (multiplicity, variations of size, hyperchromatosis), and (3) the cytoplasm (fat-filled, basophilic reaction). This procedure is quite useful for screening all unexplained gross and microscopic hematurias, questionable renal masses, or questionable lesions of the renal pelvis or calices as seen in excretory urography.

These workers also point to another very important application of this method, namely, the detection of carcinoma of the prostate gland before such a lesion is palpable in the rectum or before erosion into the urethra has occurred.

*OG-6 and EA-50 are available in bottles of 100 cc. prepared by the Gradwohl Laboratories, 3514 Lucas Ave., St. Louis 3, Mo.

The test offers no guide to the extent of invasiveness of the tumor. There is no way of grading the tumor nor of determining the point of origin of the malignant cells. Possibility of error may be present but the advantages outweigh the disadvantages.

The treatment of infections with penicillin and streptomycin has now advanced to the point where it is an everyday procedure. In order to obtain the best possible results in administering these antibiotics, dosage should be controlled by estimation of the penicillin and streptomycin level of the blood by laboratory methods. It is foolhardy to believe that these drugs may be successfully administered without this control.

ANOTHER very interesting advance in the last few years is the diagnosis of pregnancy. The generally accepted test is the Aschheim-Zondek test, using immature, female mice, based on the principle of the production of corpora hemorrhagica caused by gonadotropic hormones in urine. This gives, according to most reports, 98 to 99 per cent accurate results.

A modification of this method is that by Friedman, in which isolated mature female rabbits are used with the production of corpora hemorrhagica caused by gonadotropic hormones in urine, very similar to results obtained by the Aschheim-Zondek test. This requires twenty-four to forty-eight hours and gives an all-or-none response. It is 98 to 99 per cent accurate.

The latest method which has attracted attention is that using the *Xenopus laevis* mature female (clawed toad). This is based on the external extrusion of eggs caused by gonadotropic hormones. It may be finished in from four to twelve hours by concentration of urine, and is from 98 to 100 per cent accurate. It is preferable to the other methods because of the short time required to perform the test, its simplicity, and its economy since many tests can be made from each toad. It is for a single subcutaneous injection, no special precautions. The en- the simple observa-

tion of eggs in the water. Compared with this, the Aschheim-Zondek test requires ninety-six hours, operation, five fresh mice for each test, feeding and cleaning problem, multiple injections (forty altogether), animals must be killed, and the ovaries must be searched for in 5 animals.

The Friedman test requires thirty-six to forty-eight hours, necessitates operation, requires intravenous injection (usually two), and the rabbit is usually killed. In addition, the rabbit must be isolated and the search for ovaries carried out.

Probably the most interesting and important advance that has been made recently is that concerning the Rh blood factor. This is a phenomenon based on numerous facts connected with isoimmunization, which means immunization of a member of a species by yet another member of the same species. The discovery of the Rh factor has done much to explain many untoward transfusion reactions commonly called hemolytic reactions. Landsteiner and Wiener deserve great credit for their discovery of the Rh factor and an explanation of its reactions in retransfusions.

Landsteiner and Wiener in 1937 detected the presence in the blood of monkeys a factor which they subsequently called Rh. In using animal blood instead of human blood for preparing antisera they discovered that some of their antisera for rhesus monkey blood contained an agglutinin reacting with the blood cells of 85 per cent of the white population, quite independently of the blood groups or M, N, and P factors. In 1939 Peters and Wiener found 3 cases of hemolysis following transfusions of blood of the homologous groups, which were proved to be due to isoimmunization to the rhesus factor. Thus, this new blood factor became clinically very important and cases were reported. Wiener stated in his Alvarenga Prize lecture that this was the reason why the Rh factor, found by Landsteiner and Wiener in 1937, was first announced in January 1940. Briefly, the blood cells of 85 per cent of all white individuals are agglutinated by the anti-rhesus sera, and these contain the Rh ag-

glutigen. Such individuals are called Rh positive, while the remaining 15 per cent are called Rh negative.

IN CONNECTION with blood transfusion, Wiener demonstrated that the Rh agglutigen is antigenic to man. Thus, while Rh negative individuals can be safely transfused with Rh positive blood, they may become sensitized to the Rh factor as a result of the transfusion, and cannot again safely receive Rh positive blood. Therefore, it is preferable to transfuse Rh negative individuals with Rh negative blood. Preferably, use ORh negative blood or Rh negative blood compatible with the special blood group of the recipient. It has been properly recommended that all females, no matter at what age they require transfusions, be Rh tested, even though it is the first transfusion. If they are Rh negative and are transfused with Rh positive blood, they may develop some degree of anti-Rh antibodies. These qualities may persist for an indefinite period so if another transfusion is required and Rh positive blood is used, severe transfusion reactions may occur. It must also be kept in mind that these Rh negative females, who have been transfused at some time in early life with Rh positive blood, are isoimmunized to the Rh factor; when undertaking marriage and becoming pregnant, if the fetus is Rh positive, they will most certainly have severe intragroup transfusion reactions. If the fetus is Rh positive their chances of bearing normal infants are practically nonexistent.

The Rh types are hereditarily determined, the Rh factor being transmitted as a single Mendelian dominant by a pair of allelic genes, Rh and rh. Since every individual possesses a pair of genes from every series of allelic genes, one being derived from the mother, and the other from the father, there are three genotypes possible. Rh negative individuals are always homozygous; Rh positive individuals may be either homozygous or heterozygous. Therefore, two Rh negative parents can have only Rh negative children. If one parent is Rh nega-

tive, and the other is Rh positive, the children will all be Rh positive if the Rh positive parent is homozygous. If the Rh positive parent is heterozygous, there is equal chance that the children may be Rh positive or Rh negative; or, as it is usually stated, one-half of the children will be Rh positive and one-half will be Rh negative. When both parents are Rh positive, all the children will be Rh positive, except when the parents are both heterozygous, in which case one-fourth of the children will be Rh negative.

Rh negative individuals may become sensitized to Rh antigen in one of two ways: (1) sensitization may result from a transfusion of Rh positive blood, or (2) in women, sensitization may result from pregnancy with an Rh positive fetus. Sensitization by either of these methods may result in a serious hemolytic reaction if transfusion with Rh positive blood is given. Therefore, all Rh negative women who are to be transfused must be given only Rh negative blood.

Levine in 1940 noted that sera of patients who had had repeated miscarriages or abortions contained atypical isoagglutinins related to the Rh factor. In 1941 Katzin found that the serum of the patient previously described by Levine and Stetson agglutinated the same cells as the newly discovered anti-rhesus rabbit serum. Levine, Katzin, and Burnham called attention to the fact that a diagnosis of erythroblastosis fetalis had been made on some dead fetuses which came from the union of Rh positive and Rh negative parents. Vogel noted the majority of the mothers had Rh negative blood.

It is plausible, therefore, to accept the doctrine that Rh positive fetal cells entering the maternal blood stimulate the formation of anti-Rh agglutinins; such agglutinins, passing back to the fetus, agglutinate and destroy the fetal erythrocytes. The only barrier between the fetus and the mother is the fragile wall of the placental villus. Normally the blood of the child circulates inside the villus, while the maternal blood circulates outside this delicate structure. Osmosis may occur through this wall. The placenta is extremely susceptible to the ef-

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ket and most laboratories are equipped to make these tests with exactitude and punctuality.

TREMENDOUS interest has been aroused in this country in connection with the laboratory diagnosis of tropical medical and parasitologic cases. World War II is largely responsible for this. We projected out frontiers all over the world and our Service personnel came in contact with many diseases hitherto not seen by American physicians. Our Army and Navy medical personnel had unusual opportunities to become proficient in the study of these diseases. Many of these cases returned to our shores, some still remain under military medical supervision, others have been released to become the subjects of study of civilian physicians. Rapid transportation by air, too, has been a means of conveying to the United States diseases hitherto not seen.

It is necessary at this time to emphasize the importance of carrying out blood and stool examinations of many patients. The use of concentrated methods offers us an opportunity of obtaining a high percentage of accurate diagnoses. The thick drop of blood hemolyzed and stained with Giemsa stain is a concentrated method for investigation of the plasmodia of malaria, trypanosoma, leishmania, spirocheta of relapsing fever, microfilaria, etc. There are many concentration methods to aid in the search for eggs, larvae, and cysts. All are based on the use of a large amount of fecal material which is rendered homogeneous with water or saline solutions and screened. Cysts, eggs, and fine forms pass through the screen and are collected and centrifuged. They can then be found in the sediment.

Many concentration methods are carried out with solutions of a density below that of the eggs and cysts—Teleman and its modifications, method of Carles and Barthelemy, etc.—concentrating the eggs and cysts at the bottom of the tube. Others use solutions of a higher density than that of the eggs, the superficial portion of the fluid then being examined.

The various methods commonly used are

(1) the method of Fuelleborn, (2) the method of Teleman, which is suitable for all eggs, (3) the acetic acid and ether concentration method, (4) the Tulane method of concentration worked out by Faust, Tobie, and others. This embodies the dilution of feces in 10 parts of water strained through wet cheesecloth, centrifugalization, pouring off of supernatant fluid, adding water, centrifuging again, adding 3 to 4 cc. of a solution of zinc sulfate with a specific gravity of 1.180, shaking, centrifuging, and using the top portion for examination. (5) Baroody's modification of the Faust method for concentration of cysts and ova is also advantageous. His method differs from that of Faust in that he uses larger amounts of stool and in this way succeeds in finding cysts and eggs where one fails to do so with the original Faust method. His modified technic is a combination of Baroody and Most's centrifugal sedimentation method.

In this modification, 10 gm. of feces are placed in a 125 cc. Erlenmeyer flask containing about 75 cc. of warm water (about 40° C.); stopper the flask and shake until emulsified.

Strain through a layer of wet gauze into a 50 cc. centrifuge tube (teated bottom).

Centrifuge for one minute at 2,500 r.p.m. and pour off supernatant fluid. Add warm water to the sediment from a regulated faucet (force of the water will disperse the fecal particles and cleanse them) and centrifuge again at the same time and speed. Decant supernatant fluid; repeat one more washing and centrifugation; again decant supernatant fluid.

Add about 10 cc. of warm water and agitate sediment by shaking; then pour quickly all of contents into a 15 cc. centrifuge tube. Centrifuge for one minute at 2,500 r.p.m. and decant supernatant fluid.

Add about 10 cc. of zinc sulfate solution (33 per cent, specific gravity 1.180) to the sediment and stir with applicator sticks. Add zinc sulfate nearly to top of tube. Centrifuge for one minute at 2,500 r.p.m. Ova and cysts will float to the surface.

Take several loopfuls (bacteriologic loop) from surface and place on slide; add 1 drop of

fects of tumors, trauma, and disease. Therefore, trauma, which is seen later in scars of the placenta, permits hemorrhage of fetal blood cells into the maternal circulation. In this way, they are carried into the uterine veins and into the general circulation of the mother, constituting the mechanics of transfer of blood cells between fetus and mother.

It is believed that the mating of Rh negative women with Rh positive husbands, occurring once in 10 marriages, results in congenital hemolytic disease because of the phenomena already explained. About one in 25 Rh negative women become sensitized when bearing an Rh positive fetus. The first child is rarely affected, because it takes at least one pregnancy and sometimes more before a sufficient degree of sensitization develops. In most cases where the first-born was affected, a careful history revealed that the women had previously received a transfusion of Rh positive blood.

Summarizing the facts relating to the Rh factor:

1. *In retransfusions*—If the recipient is Rh negative and the donor is Rh positive, the Rh agglutinin in the donor's blood cells acts as an antigen and stimulates the formation of anti-Rh agglutinins and hemolysins in the patient's serum. The patient is now isoimmunized to the Rh factor. If this patient is again transfused with Rh positive blood cells, the anti-Rh antibodies, which result from the first transfusion, then agglutinate or hemolyze the incoming donor cells, resulting in a transfusion reaction or death. Therefore, always use Rh negative donor blood in retransfusions into Rh negative recipients.

2. *In primary transfusions of pregnant and postpartum women*—With an Rh negative mother and an Rh positive father, the fetus will probably be Rh positive. Through osmosis, or traumatic placental leaks, Rh positive fetal blood seeps into the mother's circulation, causing the mother to form anti-Rh antibodies in her blood serum. She is now isoimmunized to the Rh factor. If this woman is given a

transfusion with Rh positive blood, the anti-Rh antibodies now present in her blood plasma react with the incoming donor blood cells and agglutinate them or hemolyze them, or both, resulting in a transfusion reaction or death. Therefore, always transfuse Rh negative pregnant or postpartum women with Rh negative blood.

3. *In erythroblastosis fetalis*—The fetus will most likely be Rh positive if the mother is Rh negative and the father is Rh positive. Through seepage of blood into the maternal circulation, the mother's blood forms anti-Rh antibodies. Through imperfections in the placenta, the mother's blood now re-enters the fetal circulation, hemolyzes and agglutinates the Rh positive cells, and also attacks the hematopoietic system. As a result, the fetus is either expelled as an abortion, is macerated, is stillborn, or, if born alive, is erythroblastotic. If the infant is transfused with Rh positive blood cells, the anti-Rh antibodies in the infant's blood, derived from the mother, react with the incoming Rh positive donor blood cells. If the infant is transfused with blood from the mother, the anti-Rh antibodies, present in the mother's blood as a result of isoimmunization, attack the Rh positive blood cells of the infant, causing a transfusion reaction or death of the infant. The transfusions to be carried out in erythroblastotic infants should always utilize Rh negative blood.

The present tendency, therefore, in regard to safe blood transfusion, is to investigate all bloods for the Rh factor. In the primary examination of pregnant women, the practitioner must investigate the bloods of both parents with the idea of estimating isoimmunization with resultant disturbances in the child or possible death of the fetus. Some likelihood of the degree of the isoimmunization may be ascertained, assuming the mother is Rh negative and the father is Rh positive, if estimation of the anti-Rh qualities of the mother's blood is made during pregnancy.

There are various methods of determining the Rh factor, using both test tube and slide methods. Reliable testing sera are on the mar-

and were under observation for the evaluation of the success or failure of various forms of therapy. They found 10 patients positive by direct examination of fecal material free of grossly visible blood or mucus. Positive results also were obtained in water centrifugal flotation. In addition, 39 patients were found positive by the latter method or a relative efficiency of 4.9 to 1 for this method compared to direct smear examination. Such patients, having all been Army personnel diagnosed overseas or in this country, had received one or more courses of treatment. Therefore, by direct smear examination the infection would not have been detected if no mucus or blood were present in the stools. Conditions of this test naturally would simulate those faced by physicians and laboratories in civil or veterans' facility practice.

As compared with the zinc sulfate flotation method, 600 patients with schistosomiasis had been examined by the Baroody and Most method and eggs of *S. japonicum* were found in 226 patients, but in no case was the diagnosis made by zinc sulfate. In 2 specimens, wrinkled masses of eggshells were found by zinc sulfate, but proper identification was impossible.

In reference to the brine flotation method, no patients with schistosomiasis japonica were discovered although the method was applied at least once in all patients.

So far as the acid ether method is concerned, there was an efficiency with this method of only 0.32 compared to water centrifugal sedimentation (1.00).

THE WATER centrifugal sedimentation method is simple and rapid, requiring no chemical reagents, and only a minimum amount of standard laboratory equipment. The method is to be recommended especially in treated cases, particularly when the other concentration methods have been tried and have proved unsuccessful.

Attention must also be called to the advances

in the laboratory diagnosis of rickettsiosis caused by Rickettsiae or small bodies which have been proved to cause a number of very important diseases, not all of which are tropical. For instance, Rocky Mountain spotted fever has been found in many places in addition to Montana. Rickettsial diseases are those in which an animal reservoir or vector is important in the maintenance and transmission of the disease. Experimental behavior of this disease in laboratory animals constitutes one of the important means of diagnosis. We refer especially to the following rickettsial diseases: Q fever, classical typhus, murine typhus, and macular typhus in the Rocky Mountains, Colombia, Brazil, and Mexico, and also boutonneuse rickettsia, and the maculopapular rickettsia. In all of these, the use of animals is one of the important laboratory methods.

A number of serologic reactions are helpful in the diagnosis of rickettsial diseases, notably the use of the culture of *Proteus* X, namely, *Proteus* X₂, *Proteus* X₁₀, and *Proteus* XK, the last being a spontaneous variant of X₁₀. Complement fixation is important in diagnosis of many of the conditions.

The laboratory technic in the study of rickettsioses embraces (1) isolation of the virus in guinea pigs by injecting 10 cc. of venous blood from the patient; (2) the isolation of the virus in lice; (3) inoculation of fertile eggs; (4) the Weil-Felix reaction above noted, utilizing cultures of *Proteus* X₂, OX, and OXK; (5) the agglutination reaction of Weigl using a rickettsial antigen; (6) serum of Giraud, and (7) staining of the rickettsia using the Giemsa method.

For histologic section, the Woback method is used. The Castellanos method is also used in staining, as is the Macchiavello method. The Craigie method calls for the use of alkaline thiamine. Rickettsial cultures *in vitro* are very important in diagnosis and the complement fixation test reaction is used with the sheep hemolytic system, and antigen made from eggs.

D'Antoni's or Lugol's iodine and cover with a cover slip. Examine for ova of helminths and cysts of protozoa under low-power objective of microscope.

IT WILL be noted that in this method a much larger sample of feces is utilized, thereby increasing the possibility of detection in lightly infested cases or if cysts and ova are rare in the stool. Cysts may exist in "packets" and can be missed from a remote small section. Secondly, the use of warm water (about 40° C.) has advantages over the use of regular or so-called cold water. The use of warm water eliminates a high percentage of the scum which has been observed when cold water was used.

Baroody and Most worked out what, in our opinion, is the best method for finding *Schistosoma japonicum* eggs, as follows:

1. Place from 10 to 15 gm. of the feces in a 125 cc. Erlenmeyer flask containing about 100 cc. of lukewarm tap water. Insert a No. 4 rubber stopper and shake vigorously for one or two minutes, or until the particles are in fine suspension.

2. Strain the emulsified feces through two layers of wet gauze into a 50 cc. centrifuge with teated bottom (tube dimensions: height, 4¾ inches; diameter, 1 inch).

3. Centrifuge at 1,500 r.p.m. for thirty seconds (brake of centrifuge applied gradually).

4. The supernatant fluid is decanted and tap water of about 40° C. is added to the 50 cc. mark. Insert a rubber stopper and shake several times until the sediment is finely dispersed. The warm water causes a scum to rise to the surface. This is desirable.

5. Repeat procedures 3 and 4 until the supernatant fluid is clear; three washings and three centrifugations are usually sufficient.

6. After the last washing and centrifugation the clear supernatant fluid is poured off and the packed sediment remains. If the finger is gently tapped against the side of the tube, the packed sediment is dispersed and settles to the bottom of the tube by gravity within a minute.

7. With a rubber-bulbed pipette, place 4

drops of mixed sediment on a glass slide and cover with a large cover slip size 22 by 50 mm. Make at least two slides.

8. Examine under low-power objective of the microscope for eggs of schistosoma. *S. japonicum* eggs are oval, 70 to 100 by 50 to 60 microns, may or may not have a rudimentary spine, and in blue-white light appear greenish orange. *Schistosoma mansoni* eggs are elongated, 114 to 175 by 45 to 68 microns, and have large lateral spines. In both species, if the ova are visible, the miracidia will exhibit movements within the eggshells, and the activity of the flame cells may be seen under higher magnification.

9. If the slides are negative for schistosoma ova, add about 10 drops of water to the remaining sediment in the tube, leave overnight in a warm place, and examine the following day for miracidia. The entire contents of the tube can be placed on a large slide and examined under a dissecting microscope. This phase of the examination takes less than two minutes.

10. Excluding procedure 9, not more than five minutes are required for the examination of each slide, and not more than from fifteen to twenty minutes are required for procedures 1 through 8.

Summary of the method—(1) A large sample of the feces is used; this is especially valuable in light infections; (2) viability of the ova is determined; (3) rapidity of method—report can be rendered within fifteen minutes; (4) a hatching test is part of the method; (5) other ova, cysts of protozoa, and larvae of helminths may also be found and identified (for protozoan cysts, add a drop of Lugol's or D'Antoni's iodine to slide); (6) preserved concentrated specimens can be made quickly by adding 10 per cent formalin to the sediment in the tube at the end of the fresh examination; (7) no chemical reagents are required; minimum standard laboratory equipment is used.

Baroody and Most compared the direct smear examination and their water centrifugal sedimentation method by examining 1,026 consecutive fecal specimens simultaneously. These patients had all received treatment previously

Of these lesions, intra-articular fracture of the neck of the femur is by far of the greatest importance. The principal blood supply to the head of the femur comes by way of neck capsule branches of the anterior and posterior circumflex arteries, and when the neck is fractured near the head, all or most vessels may be severed regardless of the extent of the displacement of fragments. As a result, there is immediate cutting off of the blood supply to the major portion or all of the head of the femur. In some cases, the arteries coming by way of the round ligament are of sufficient size to maintain the circulation of the head, but more frequently they provide it with little blood supply, and if the neck is fractured the head becomes necrotic.

If the head becomes necrotic and nonunion follows^{5,6} the blood vessels grow in by way of the round ligament, of untorn portions of the capsule and of adhesions and slowly invade the dead bone, usually of the inferior portion of the head and in the vicinity of the fovea. They are accompanied by a fibrous callus which invades the cancellous spaces and in its deeper portions undergoes metaplasia and absorbs and replaces the dead bone and dead marrow by new bone and living marrow. The old dead bone, having no blood supply, cannot atrophy, and retains its original density as revealed by roentgenograms.

The living bone of the distal fragment gradually undergoes atrophy as a result of the marked disuse produced by the ununited fracture. Consequently it comes to cast a fainter shadow than the dead bone of the head or any newly formed bone in the head since the latter is spongy as a result of being deposited in an ununited nonfunctioning head.

This combination of atrophy in the distal fragment and of spongy bone in the transformed lower portion of the dead head makes it possible to recognize the necrotic portion of the head by the greater density of its shadow cast in roentgenograms. If the ununited fracture is left untreated, the dead bone may be slowly replaced by living bone so that within two or three years only a small amount of it remains,

usually in the upper portion of the head. But the dead portion never collapses since, because of the nonunion, it is non-weight bearing. The articular cartilage, being deprived of its nutrition by tissue fluid derived from the blood supply of the underlying bone, undergoes extensive necrosis, and in the course of time is invaded by blood vessels and fibrous tissue, and very slowly replaced by a layer of fibrocartilage.

THE management of a necrotic head with nonunion depends on the duration of the fracture at the time when treatment is begun. If seen within the first one or two years while the head consists mainly of necrotic bone,⁷ the fracture may be openly reduced through a Smith-Petersen incision, the fragments fixed by one or two rectangular tibial bone grafts inserted from the side of the shaft across the neck through the entire length of the upper portion of the head, and by threaded wires or screws similarly inserted from the side obliquely upward into other portions of the head.

The drilling of the upper portion of the head gets rid of a considerable amount of dead bone and opens the remaining portion for rapid invasion of the empty space alongside the rectangular grafts by callus and replacement by new bone. The grafts serve as struts to prevent collapse of the upper portion of the head and greatly increase the frequency of healing of the fracture of the neck. By this procedure the dead head may be transformed into living bone and the dead articular cartilage replaced by fibrocartilage with the preservation of the normal contour of the head and the reestablishment of a well-functioning hip. A tubular drill may be used for tunneling the head portion and the core saved as a biopsy for microscopic examination.

If the nonunion is of two or more years standing and the dead bone and dead articular cartilage have been extensively absorbed and replaced by frail new bone and fibrocartilage respectively, it is best to excise the head and perform either one of the various types of arthroplasty or an arthrodesis of the hip.

Aseptic Necrosis of Bone Management and Prognosis

DALLAS B. PHEMISTER*

UNIVERSITY OF CHICAGO SCHOOL OF MEDICINE, CHICAGO

BONE undergoes aseptic necrosis as the immediate result of injury or occlusion of the blood vessels in the absence of infection. As in a case of infarction of the soft parts, the devascularized tissue dies within the course of a very few days. The idea that the bone may not die until months or years after the injury or vascular blockage is wholly fallacious and is the result of assumption that death occurs at the time when differences in density between necrotic and living portions become recognizable in roentgenograms, or when a dead articular portion breaks down from weight-bearing, both phenomena being late manifestations of aseptic necrosis.

The most frequent cause of aseptic necrosis from injury is fracture, but it may also be produced by dislocation, as of the hip, wrist, or ankle joint; by operation, as arthroplasty of the hip, or extensive stripping of fragments in the operative treatment of fractures.¹ A rare cause appears to be sprain or direct trauma to the nutrient vessels as in the case of the carpal lunatum.

Occlusion of the blood vessels of bone result-

ing in aseptic necrosis^{2,3} may be produced by embolism, thrombosis, or localized obliterative vascular disease frequently of an obscure nature, but sometimes on an arteriosclerotic basis.

Fracture of the shaft of the long bones causes a certain amount of necrosis of the cortex of the ends of the fragments and of splinters, but bony union usually occurs in such cases in normal time since the callus is laid down by surviving periosteum and endosteum and the dead bone is subsequently replaced by new bone by a gradual process of creeping substitution. When the fracture involves the end of the bone and the shorter fragment is either entirely or mainly within the joint, its entire circulation may be cut off, leading to necrosis of the bone, marrow, and the articular cartilage. In such cases the callus can be laid down only by the end of the shaft fragment instead of by both fragments, and the incidence of nonunion is thereby appreciably increased.

Aseptic necrosis from fractures bordering on joints is seen most frequently in the head and neck of the femur, the carpal navicular bone, the lunatum, the astragalus, the capitellum of the humerus, and the head of the radius. Smaller necrotic lesions bordering on the articular surface of various joints may be separated by the trauma of usage and give rise to the picture of osteochondritis dissecans.

*Thomas D. Jones Professor Emeritus, Department of Surgery, University of Chicago School of Medicine, Chicago.

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Large to small infarcts are found less frequently in the shafts of humerus, femur, and tibia, and rarely in the fibula. The infarcts of the shaft are gradually invaded about the periphery by blood vessels and fibrous tissue with properties similar to callus. They occupy the cancellous spaces and absorb the dead marrow and cancellous trabeculae, replacing them by living trabeculae and living marrow.

This creeping replacement of the dead bone by new bone may go on over periods from months to two or three years, and it may involve inner portions of cortex which has lost its circulation. Small infarcts may be completely replaced. But with large infarcts when the replacement process has advanced to the point at which the new bone is strong, the reparative stimulus may be exhausted. Large to small areas of dead bone may be left permanently, and calcification of the fibrous zone of invasion about the periphery and of scant small islands of the interior may come about much as in the case of old infarcts of the spleen or kidney. Infarcts of the diaphyses produce little or no symptoms and are not recognizable in roentgenograms until years after formation when the calcification casts heavy shadows in roentgenograms that are characteristic of the lesion.

Aseptic necrosis of the head of the femur usually involves the entire structure including bone and its overlying cartilage, although in some instances small portions of the lower part of the head appear to remain alive. Following the occurrence of embolism, there is gradual invasion of the dead bone of the head by blood vessels and callus-like tissue coming from the neck and sometimes from the round ligament with replacement of the dead bone and dead marrow by living bone and living marrow similar to that which is described for infarcts of the shaft.

Single or, more frequently, multiple infarction of epiphyses and diaphyses similar to that produced by caisson disease may be produced by vascular occlusion from other causes, most of which are very obscure.⁴ In some cases the lesions develop in elderly individuals affected by cardiovascular disease, and obliterative ar-

teriosclerosis may be the direct cause of the infarction. There is little evidence that multiple arterial embolism has been the exciting cause in the few cases that have come to autopsy, since embolic infarction of the soft tissues which might be expected as an accompaniment has not been found. Rheumatic fever and rheumatic heart disease may have been the exciting cause in one case studied. Single or multiple infarction has been accompanied by degenerative arthritis in joints remote from the lesions with sufficient frequency to suggest an etiologic relationship between the two conditions. Further studies will be necessary before the causes of multiple nontraumatic aseptic bone infarction are understood.

THE clinical course and management of necrosis of the head of the femur are much the same whether in fractures of the neck of the femur followed by bony union, dislocations of the hip, or nontraumatic lesions such as caisson disease and obscure obstructive arterial disease. The callus-like fibrous tissue which grows from the neck into the dead head slowly absorbs and replaces the dead bone by new bone. During the initial stages of invasion and replacement, the changes proceed asymptotically and there is little interference with function of the hip. The head of the bone retains its contour and density and the condition can usually not be recognized in roentgenograms.

After several months to a year or two the invasion in all of these conditions reaches the weight-bearing part of the head from the lateral and inferior portions, and as the stress from the acetabulum is thrown upon the zone of replacing new bone, it fractures because it is at first weaker than the old dead bone which it has replaced.⁵ The broken off portion of dead bone lying beneath the acetabulum then begins to collapse from further weight bearing. If roentgenograms are taken as soon as the hip becomes painful, the occurrence of the fracture may be recognized early while there is extremely little displacement, and the opportune time

In case of a fresh fracture of the neck with death of the proximal fragment, bony union usually follows if the fragments are either impacted or well reduced and well fixed as by a Smith-Petersen nail or threaded pins. The callus and blood vessels grow from the distal fragment across the fracture line into the dead end of the neck and from there gradually invade the head, the dead bone being slowly replaced by new bone. At the fracture site the callus usually ossifies in the course of two to three months. If the patient is kept off the feet for a prolonged period up to as much as two or three years, the dead bone may all be replaced by new bone without collapse of the weight-bearing portion of the head from pressure against the acetabulum, and a well-functioning hip is re-established.⁸ However, if weight-bearing is permitted, the portion of the head underlying the acetabulum will be broken off when, many months after the fracture, the invading new bone reaches its margin because the zone of replacing new bone is temporarily soft and too weak to stand the pressure. The collapse of the remaining dead portion leads to deformity and degenerative arthritis and a poor functional result.

The broken-off dead portion may eventually become reattached and replaced by new bone, or occasionally it remains practically unchanged with an ununited fracture line separating it from the underlying bed similar to the loose body from the femoral condyle in osteochondritis dissecans at the knee. In a certain percentage of cases of fracture of the neck with aseptic necrosis in which pin or nail fixation is employed, the fracture fails to unite and the neck is slowly eroded and shortened. In other cases, the fracture unites but months later a re-fracture occurs a short distance proximal to the old fracture line as weight is thrown upon the weak invading zone of new bone.

The roentgenographic recognition of a dead head produced by fracture of the neck is much more difficult if the fracture unites than if it remains ununited.⁷ This is because when the fracture unites and the limb is used, there is little or no atrophy of disuse of the distal liv-

ing fragment and its density remains almost the same as that of the dead head which cannot atrophy. On the other hand, in case of non-union there is little use of the extremity and marked atrophy of disuse of the distal living fragment which in consequence casts a much fainter shadow than that of the dead head.

Aseptic necrosis of bone produced by lesions other than tearing the blood vessels in injuries is relatively common in certain epiphyses and short bones during childhood and adult life. Familiar examples are Legg Perthes' disease of the hip, Osgood-Schlatter's disease of the tibial tubercle, Köhler's disease of the tarsal navicular and the metatarsal bones, and Calvé's disease of the vertebral bodies. These lesions form a special group and will not be further considered here.

NONTRAUMATIC aseptic necrosis is less frequent in adults than in children and presents a somewhat different clinical picture. The etiology in the majority of the cases is obscure. Best known cause is caisson disease³ in which the excess nitrogen taken up by the blood and tissue fluids during the period spent by the worker in compressed air is liberated as a gas when decompression is too rapidly effected.

The exact method in which the gas acts upon the bones is imperfectly understood. It may be through arterial embolism or through direct pressure on the bone marrow which is rich in fat and absorbs the nitrogen in large quantities. The lesions are located in the long bones of the extremities and may affect either epiphysis or diaphysis, and not infrequently both epiphysis and diaphysis of one or several bones. The most frequent sites are the head and neck of the femur, the head of the humerus, the lower end of the femur, the upper and lower ends of the tibia, and the upper end of the shaft of the humerus. The bones of the trunk and the short bones of the extremities are practically never involved.

Large infarcts bordering on the articular cartilage are common in the head of the femur and humerus and are frequently bilateral.

Large to small infarcts are found less frequently in the shafts of humerus, femur, and tibia, and rarely in the fibula. The infarcts of the shaft are gradually invaded about the periphery by blood vessels and fibrous tissue with properties similar to callus. They occupy the cancellous spaces and absorb the dead marrow and cancellous trabeculae, replacing them by living trabeculae and living marrow.

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for treatment is then at hand. If further weight bearing is permitted, the broken off dead bone will be downwardly displaced, the head gradually deformed, and degenerative arthritis set up.

Patients with beginning collapse of the head have been placed on crutches and forbidden weight bearing over long periods up to two or three years, but despite this drastic therapy the head usually flattens to some extent and deforming arthritis is established, leaving a poorly functioning hip. The ideal treatment in this early stage of recognition should aim at the prevention of further collapse of the head and rapid replacement of the dead bone by new bone and of the dead articular cartilage by fibrocartilage.

Recently in a limited number of cases, an operation has been employed similar to that described for ununited fracture of the neck with death of the head which has yielded results superior to those obtained by most of the methods in common practice. The lateral surface of the shaft is exposed through a 6-inch incision extending downward from the greater trochanter. With x-ray control, a 1 cm. drill hole is made extending obliquely upward and inward through the upper portion of the neck and head, perforating the overlying articular cartilage. A second drill hole is started about $2\frac{1}{2}$ cm. below the first and directed slightly more obliquely upward so that it perforates the articular cortex and cartilage approximately 1 cm. below the first drill hole. If a Smith-Petersen nail has been used and the fracture has united but the head has later collapsed, the nail is removed and the second drill hole is made through its channel. Two bone grafts, each 1 cm. broad and the length of the tunnel, are taken from the anteromesial surface of the tibia and inserted sagittally into the tunnels ending just short of the articular surface.

The wound is closed and the patient is kept on crutches for nine months to a year depending on the clinical course and the appearance shown in roentgenograms. The drill removes a considerable portion of the dead bone. The grafts act as strong struts to prevent collapse of the upper portion of the head during the period

of invasion and replacement by new bone. There is room between the walls of the round holes and the rectangular pegs for the ingrowth of blood vessels and callus from the neck side into the remaining dead bone of the head. This brings about a relatively rapid invasion and transformation of what is left of the dead head, and fibrous tissue grows out of the proximal end of the hole onto the articular surface, invading, absorbing, and replacing the dead articular cartilage by fibrocartilage.

Thus a head of normal strength and contour, covered by living cartilage, is relatively rapidly created, and degenerative changes in the hip joint are reduced to a minimum. Patients treated this way have an excellent clinical result characterized by freedom from pain with almost a normal range of motion and good weight bearing after one year.

If the patient is not seen until late when the head of the femur is markedly broken down and the joint is badly crippled, an operation may be indicated, such as a vitallium cup or other arthroplasty or arthrodesis of the hip joint.

NECROSIS of the proximal and/or rarely the distal fragment of the carpal navicular results from fracture of that bone in a considerable percentage of the cases. It predisposes to nonunion and may be diagnosed after the lapse of a few weeks by the presence of greater density in the dead fragment than in the atrophied living fragment and the surrounding wrist bones. Early treatment by an intramedullary bone peg leads to bony union and replacement of the dead bone by living bone with less tendency to the establishment of degenerative arthritis in the carpus than is seen in the old neglected cases or in long-standing necrosis of the navicular bone.⁹

When the neck of the astragalus is broken, the blood supply of the body of the bone may be interrupted, causing death of the fragment. In exceptional cases the distal fragment may also become necrotic which predisposes to nonunion.¹ Necrosis usually leads to more or less

breaking down of the body fragments and degenerative arthritis which may be so severe that arthrodesis of the ankle may be called for. Similar changes including loose bodies may re-

sult from aseptic necrosis following intra-articular fracture at other joints of the body, and plastic or arthrodesing operations may be necessary to relieve pain and improve function.

REFERENCES

1. PHEMISTER, D. B.: Changes in bones and joints resulting from interruption of circulation. I. General considerations and changes resulting from injuries. *Arch. Surg.* 41:436, 1940.
2. PHEMISTER, D. B.: Changes in bones and joints resulting from interruption of circulation. II. Nontraumatic lesions in adults with bone infarction: arthritis deformans. *Arch. Surg.* 41:1455, 1940.
3. KAHLSTROM, S. C., BURTON, C. C., and PHEMISTER, D. B.: Aseptic necrosis of bone. I. Infarction of bones in caisson disease resulting in encapsulated and calcified areas in diaphyses and in arthritis deformans. *Surg., Gynec. & Obst.* 68:129, 1939.
4. KAHLSTROM, S. C., BURTON, C. C., and PHEMISTER, D. B.: Aseptic necrosis of bone. II. Infarction of bone of undetermined etiology resulting in encapsulated and calcified areas in diaphyses and in arthritis deformans. *Surg., Gynec. & Obst.* 68:631, 1939.
5. PHEMISTER, D. B.: Repair of bone in the presence of aseptic necrosis resulting from fractures, transplantations and vascular obstruction. *J. Bone & Joint Surg.* 12:769, 1930.
6. PHEMISTER, D. B.: Fractures of neck of femur, dislocations of hip, and obscure vascular disturbances producing aseptic necrosis of head of femur. *Surg., Gynec. & Obst.* 59:415, 1934.
7. SHERMAN, MARY S., and PHEMISTER, D. B.: The pathology of ununited fractures of the neck of the femur. *J. Bone & Joint Surg.* 29:19, 1947.
8. PHEMISTER, D. B.: The pathology of ununited fractures of the neck of the femur with special reference to the head. *J. Bone & Joint Surg.* 21:681, 1939.
9. RODHOLM, A. K., and PHEMISTER, D. B.: Cyst-like lesions of carpal bones associated with ununited fractures, aseptic necrosis and traumatic arthritis. *J. Bone & Joint Surg.* 30A:151, 1948.



THE CRAMP

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Treatment of Alcohol Addiction

GIORGIO LOLLI*

YALE PLAN CLINIC, YALE UNIVERSITY, NEW HAVEN

THERE are about three million excessive, uncontrolled drinkers in this country. Of these, about 600,000 are suffering from bodily or mental, or both bodily and mental diseases resulting from excessive use of alcohol. These are the well-known diseases of chronic alcoholism. I do not think it is necessary to discuss the therapeutic procedures employed in treatment of diseases following excessive drinking over a long period of time, since these diseases are mostly due to vitamin deficiencies and their treatment is based on the awareness of their nutritional origin.

It is more important to focus attention on addiction to alcohol itself. At Yale University, work on problems of alcohol addiction had been going on for many years. In 1944 it was decided that something should be done in the line of active treatment of addiction to alcohol. In March 1944, two free clinics for the treatment of addictive drinkers were established in Connecticut, one in New Haven and the other in Hartford, as an experimental project of the Laboratory of Applied Physi-

ology of Yale University, in order to test the possibilities of large-scale rehabilitation of alcoholics at a limited cost.

Last year, as a result of legislation enacted by the State of Connecticut, the Hartford Clinic was turned over to the state. The New Haven Clinic, however, will remain under the supervision of Yale University.

I shall try to describe as briefly as possible our therapeutic procedures at the New Haven Clinic. Our staff is made up of a consultant in psychiatry, an internist with a background of psychiatric study, two social workers, a psychologist who devotes only part time to the clinic (mainly to psychologic testing), and one educator, who, because of his training, seemed particularly fit to deal with problems relating to alcohol addiction.

There were objections to the setting up of a specialized clinic for alcoholics. However, there are many indications for clinics of this type. We know, of course, that addiction to alcohol is the result of many causes. We do not know of any physiologic deviation underlying all cases of addiction. We know mainly of precipitating factors. There is no doubt that a number of addictive drinkers were treated in the past and are still treated in nonspecialized clinics, both medical and psychiatric. However,

*Medical Director, Yale Plan Clinic, Yale University, New Haven.

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it appeared justifiable to set up specialized clinics because we felt that when true addiction to alcohol is present, irrespective of the causative factors involved, there are similarities among alcoholics which justify singling them out of other groups of patients. It is sufficient to mention these similarities: Because of their socially unacceptable behavior they are more or less constantly at odds with their environment; intoxication is constantly the most obvious symptom they offer; alcohol itself represents for them the most cherished source of pleasure and at the same time the most appealing means of wiping out pain.

Because treatment at the clinic is carried out on an ambulatory basis, we have some limitations. We have to exclude patients who are severely intoxicated. We refer these cases to hospitals or to private institutions. We have to exclude all psychotic patients whose place is either in state hospitals or in private institutions. Patients who are temporarily suffering from medical diseases either due or not due to alcohol, and who require hospitalization, are also excluded.

There still remains a large number of addictive drinkers who can be adequately treated on an ambulatory basis. We feel that ambulatory treatment is preferable whenever possible, because many times hospitalization or confinement in an institution represents for the addictive drinker another way of escaping a difficult situation.

We take care of patients just out of a bout, patients in that stage which is usually labeled "hangover." Hangover is that period which begins when the concentration of alcohol in the blood falls to relatively low levels and the patient is again aware of a painful reality, and ends when the patient is back to a situation which is similar to or slightly worse than it was immediately preceding the last bout.

We feel that immediate interruption of drinking is required at this period. The patient in hangover is usually overflowed with pain, both physical and mental. Unless help is given at this stage of the addictive process, he is apt to resort again to alcohol in order to wipe out

both the physical and the mental pain. Sedation is required in most cases at this stage, but we feel that it is not sufficient. It must be immediately complemented by psychotherapy, which should begin as soon as possible.

Close observation of the patient in the hangover stage is most helpful in reaching some diagnostic impression of the main problems underlying his addiction. During this stage there is a magnification of both bodily and mental symptoms which appear more obvious than they do during intermediate periods of sobriety. Also, the patient is less aggressive than usual and is more receptive to therapeutic approaches.

WHEN the patient comes to the clinic in a period of temporary sobriety in order to achieve permanent sobriety, our approach is more or less as follows: We try to evaluate as rapidly as possible the main problems underlying the individual's uncontrolled drinking. Usually the addictive drinker faces very serious difficulties in his environment, difficulties which must be realized and evaluated at once.

The patient is given a physical examination to determine his physical condition and the possible presence of physiologic deviations. A psychologic study follows and is complemented, if necessary, by psychologic testing.

Therapy begins immediately, proceeding in some way from the periphery to the core. Our first attempts aim at the correction of environmental difficulties. Family disharmony is present in a great number of cases; so are employment problems and conflicts with the law. We often need the cooperation of other social agencies interested in this problem. It is evident to us that the greater these difficulties are, the worse the prognosis in the case. As a matter of fact, the cases that have had a long history of conflicts with the law are of very doubtful prognosis.

Following this attempt at correcting the environmental factors and sometimes parallel to it, we try to remedy all bodily disorders, whether due to alcohol or other causes. We pay

specific attention to disorders which are most often observed in individuals addicted to alcohol. An example of this is hypoglycemic fatigue, which sometimes can be corrected, at least temporarily, with proper medication. We note also the possible presence of disorders of the glands of inner secretion. Disorders of this kind are especially frequent in alcoholic women. A large group of women start drinking at menopause; their addiction can often be favorably affected by proper hormonal treatment.

The treatment of addiction itself is mainly a psychologic one. Medication can be used, but is usually only an adjuvant. Mention should be made of amphetamine sulfate, a drug which might relieve the patient of the frequent feeling of fatigue and which often gives him a sense of well-being and makes him more receptive to psychotherapy.

A strictly medical approach to the problem of alcohol addiction is the so-called conditioned reflex treatment or aversion treatment, an attempt to create an aversion to alcohol by means of injections of emetic drugs. We believe that this approach has its definite place in the treatment of alcohol addiction. However, we feel that it is doomed to failure unless complemented by psychologic approaches as soon as possible.

The psychologic approaches to the problem are many, but are all, however, based on the following assumptions: First, it is impossible to shift from an uncontrolled pattern of drinking to a controlled one. The few, not completely proved exceptions to this rule do not challenge its validity. Therefore, the aim is permanent sobriety. Second, permanent sobriety can be achieved only if corrective emotional experiences occur in the personality of the patient. There is no doubt that in many cases these corrective emotional experiences can be elicited only by a rational use of strictly psychiatric technics. We have found that a combination of individual therapy with group therapy is most helpful in many cases.

Psychotherapy, though always under psychiatric supervision, is carried out in our clinic

also by the social worker, the internist, and the educator. The educator supervises the program of group therapy.

ALCOHOLICS can also be helped by approaches other than psychiatric ones. An outstanding example of a nonpsychiatric approach to alcohol addiction is embodied in the program of Alcoholics Anonymous, an association of formerly uncontrolled drinkers who, in helping other drinkers to achieve sobriety, help themselves to keep sober. A rational analysis of the psychologic mechanisms underlying the successes of Alcoholics Anonymous shows that they employ, though on a more intuitive basis, some of those psychologic tools which are used in orthodox psychiatry, such as emotional support, persuasion, catharsis, insight, etc.

There is no doubt that other approaches, such as religion, can be helpful in some cases. It is our aim to take care by psychologic or medical means, of all those patients who cannot be handled otherwise, and to pave the way for contacts with other organizations for all those patients who can be helped outside our institution.

We feel that the program of rehabilitation of alcoholics is a very long-term proposition which requires years in many cases.

As far as our results are concerned, we see about 30 new patients each month. The clinic is completely free and patients belong to every walk of life. About 50 per cent who contact us drop out of the picture after two or three interviews. Of the remaining 50 per cent, about half achieve permanent sobriety after a period of three, four, and sometimes six months. The other half keep on drinking. However, we feel that even in these cases the clinic has had a marked impact on them. It appears that more often than not the drinking episodes are spaced and sometimes shortened, that there is a better adjustment of the addictive drinker to his family, to his job, and more important than anything else, to himself.

Middle Lobe Syndrome

EVARTS A. GRAHAM, THOMAS H. BURFORD, AND JOHN H. MAYER*

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

MIDDLE LOBE atelectasis of nontuberculous origin with suppurative changes has within very recent years been encountered with unprecedented frequency. Puzzled at first by how often the middle lobe was involved, we were struck by the logic of Brock's¹ explanation of middle lobe atelectasis in tuberculosis. This observer pointed out the strategic location of the middle lobe bronchus in relation to lobar lymph nodes (Figure 1) and showed how bronchocompression from these nodes was the causative factor in the so-called bronchostenosis and nonaeration of the middle lobe in tuberculosis. As he has re-emphasized in his splendid study of the tracheobronchial tree,² the middle lobe bronchus lies at the apex of the lymphatic pathways from both upper and lower lobes. It is then particularly vulnerable from the standpoint of lymphadenopathy impingement (Figure 1).

More recently Zdansky³ quite independently has been impressed by the vulnerability of the middle lobe bronchus to lymph node enlargement and has termed the middle lobe bronchus

a "punctum minoris resistentiae." He has demonstrated at operation middle lobe atelectasis secondary to bronchial compression by enlarged lymph nodes in nontuberculous cases.

To date we have been able to study twelve examples of bronchial compression of the middle lobe bronchus by enlarged lymph nodes in nontuberculous cases. In general, the picture clinically has been fairly consistent. Hemoptysis and recurrent episodes of pulmonary infection have been the major presenting symptoms. Only two patients in this group failed to manifest one or both of these features as their chief complaint (Table 1). Sputum, which is generally characteristic of bronchiectasis, varies in amount. Chronic cough, of course, is universally present in these patients. The onset in some cases is marked by a severe acute febrile episode usually diagnosed as pneumonia or "flu." In others, the onset is more insidious. In the intervals between episodes, the patients as a rule are not well. They complain of easy fatigability and are unable to carry on their usual work.

CASE HISTORY

I. M., 31-year-old white female, was admitted to the Barnes Hospital in 1947. She stated that her illness began six years previously with a

*From the Chest Service of Barnes Hospital and the Department of Surgery, Washington University School of Medicine, St. Louis.

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EVARTS A. GRAHAM



THOMAS H. BURFORD



JOHN H. MAYER

moderately severe respiratory infection of unknown etiology. This episode was associated with fever of approximately one week's duration. Following this she had persistent cough productive of a small amount of sputum until 1943 at which time she had another acute episode characterized by fever and prostration. After the subsidence of this episode, cough with moderate amounts of sputum continued. A third acute flare-up similar to the previous two was experienced in 1945. Productive cough continued. Occasionally the patient would expectorate blood-streaked sputum.

Physical examination revealed signs of atelectasis over the area of the middle lobe of the right lung. Laboratory findings were essentially negative. X-ray films showed a typical picture of atelectasis of the middle lobe. Lipiodol bronchograms demonstrated a block of the middle lobe bronchus, and bronchoscopy showed it to be obstructed to such a degree that not

even a small suction tip could be forced into its lumen. A biopsy of the mucosa of this area showed only chronic inflammation.

At operation a small totally atelectatic middle lobe was found, the bronchus of which seemed to be compressed by a large firm lymph gland lying on the inferior surface of the bronchus near its beginning. The removal of the lobe was followed by an uncomplicated post-operative convalescence. She has remained well for a period of sixteen months since operation.

X-ray findings—The x-ray findings were uniformly those of atelectasis of the involved lobe (Figures 2 and 5). Occasionally these shadows had been misinterpreted as being due to interlobar effusions. Lipiodol studies were not done routinely, but when done revealed either non-filling of the involved bronchus or a contracted bronchiectatic pattern.

Bronchoscopy—Bronchoscopic findings revealed marked cicatricial stenosis of the middle lobe bronchus in every case. Usually the orifice was slit-like. In any event the lumen distal to the origin of the middle lobe bronchus invariably gave evidence of definite obstruction. Depending upon the time interval from the last episode of superimposed infection, there was a greater or less degree of nonulcerative inflam-

TABLE I
PRESENTING COMPLAINTS

SYMPTOM	NUMBER OF CASES
Hemoptysis	
Recurrent pneumonitis	
Chronic cough with sputum	

matory edema and congestion about the orifice. No broncholiths or foreign bodies were found in any case. In the majority of cases, pus was found coming from the middle lobe orifice. The remainder of the tracheobronchial tree showed no significant changes.

Operative findings—At operation there was in all cases a small totally atelectatic middle lobe (Figure 3). Universally, the proximal portion of the middle lobe bronchus was compressed by enlarged, firm lymph nodes. The key node from the point of view of compression was most frequently found on the inferior surface of the bronchus. The compression was definite and unmistakable, and when the node was removed, the groove in the bronchus remained.

Pathology—Pathologically, the lobes were atelectatic, with varying degrees of interstitial fibrotic change. The bronchi were dilated and presented the characteristic changes of bronchiectasis. There was pseudostratification of the mucosa with loss of cilia. Areas of metaplasia, submucosal loss of elastic tissue, and fibrous tissue replacement of cartilage were common findings. In some cases multiple small abscesses were present in the lobe (Figure 4).

The main bronchus to the middle lobe showed cicatricial stenosis most prominent at the point of maximum compression. This point was easily correlated, since as pointed out, the enlarged node or nodes invariably left an indentation plainly visible on the external surface of the bronchus.

The lymph nodes were not remarkable except for size and consistency. In each case the nodes were markedly enlarged and firm. Histologic section showed only the changes of a chronic, nonspecific lymphadenitis.

DISCUSSION

IN TRYING to find a satisfactory explanation for the present frequency of this previously unnoted syndrome, we considered first the influence of the sulfonamides and the antibiotics. It seemed reasonable that these agents, particularly penicillin, with its known efficacy

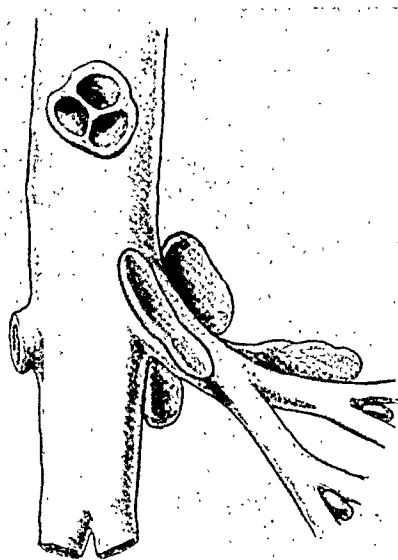


Figure 1. Diagram of middle lobe bronchus showing lymph node arrangement. Reproduced from Brock, R. C.: *The Anatomy of the Bronchial Tree*. Oxford Medical Publications, 1946. (By permission of the author and publisher.)

in pulmonary infections, and its almost universal exhibition by physicians whenever pulmonary inflammation exists or is suspected, might be responsible. Infections of the lung which in pre-penicillin years went on to fatal pneumonias or which suppurated to give frank lung abscesses might well now be so attenuated that a less fulminating picture supervened. The previously mentioned contribution of Brock which so admirably explains the bronchial obstruction very nicely completed the picture. Unfortunately, when a sufficiently large series had been accumulated, a careful scrutiny of the case records failed to demonstrate any relationship between the lesion and penicillin, nor indeed was any etiologic common denominator apparent.



EVARTS A. GRAHAM



THOMAS H. BURFORD



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TABLE I
PRESENTING COMPLAINTS

SYMPTOM	NUMBER OF CASES
Hemoptysis	7
Recurrent pneumonitis	3
Chronic cough with sputum	2



Figure 3. View at operation showing atelectatic middle lobe.



Figure 4. Resected middle lobe showing lung abscess secondary to obstruction.

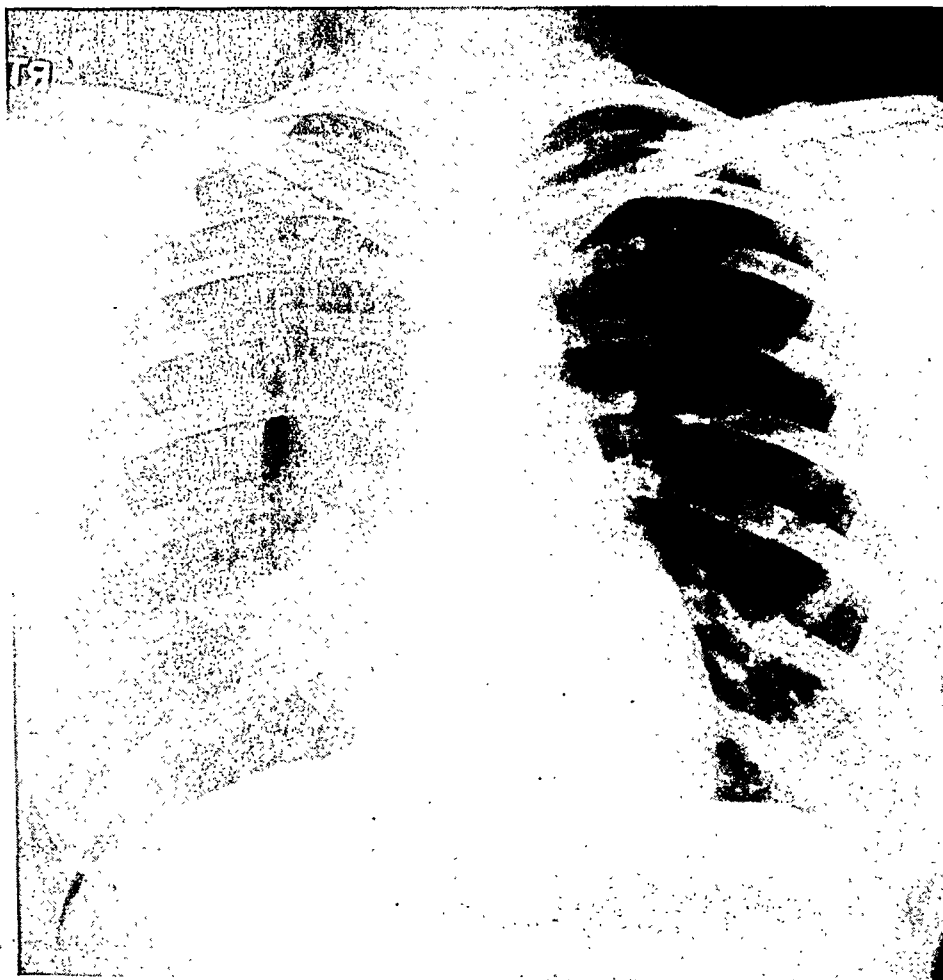


Figure 2. X-ray of typical middle lobe atelectasis showing PA view.

IN THIS group of twelve cases there were only three to whom penicillin had been administered at the time of the initial episode. In five of the cases penicillin had never been given prior to coming under our observation. It is thus impossible to make out a case for penicillin attenuation of otherwise lethal or frankly suppurative infections.

That the atypical or virus pneumonias might be responsible also lacks any real confirmation. While this disease not infrequently results in delayed clearing of areas of lung as demonstrated by physical findings, and x-ray, these areas of residual infiltration are patchy and an exhaustive review of the literature has failed to reveal evidence that the persistent areas last longer than several weeks. Moreover, the pa-

tient with a residual opacity following virus pneumonia is clinically well and never manifests the signs and symptoms secondary to bronchial obstruction. To our knowledge, no one has reported persistent middle lobe atelectasis following atypical virus pneumonia.

A very critical examination of the pathology as well as the clinical histories of the patients reported in this series fails to give a clue as to why this lesion had not generally been seen more frequently in the past. It is altogether likely that no single factor is responsible but that any inflammatory process which leads to lobar hilar lymphadenopathy may be followed by bronchocompression, bronchostenosis, and middle lobe atelectasis. Certainly once the lymphadenopathy has developed, the essential

Treatment of Diseases of the Thyroid

GEORGE CRILE, JR.*

CLEVELAND CLINIC, CLEVELAND

IN THIS clinic I should like to emphasize the rationale of the treatment of hyperthyroidism, whether this treatment be medical or surgical, and point out some of the indications for thyroidectomy in the treatment of various types of goiter. As a case study we have a patient who illustrates some of the fundamental signs and symptoms observed in early hyperthyroidism.

The patient is 44 years of age. Her symptoms are of particular interest as she did not know that she was sick at all. She entered the hospital because of a completely different complaint, and, during the course of routine examination, objective signs of early hyperthyroidism were observed. She was found to have a small diffuse goiter. She was nervous, although she had hardly paid any attention to it herself, and it was noted that she had a persistent tachycardia while at rest.

It is significant that this patient did not realize that she was sick; yet she had hyperthyroidism. A sensation of illness is not characteristic of early hyperthyroidism. I think one must beware of patients who complain of fatigue, of prostration, of nervous exhaustion, and who

have symptoms suggestive of hyperthyroidism without the signs. Hyperthyroidism, after all, is an organic disease; it is a disease in which the entire metabolic system of the body is deranged. Hypermetabolism is characteristic of this disease, and hypermetabolism expresses itself in a stimulation of the circulatory system and by other manifestations which are objectively evident, as with the patient now under discussion.

The goiter here is not large. It is barely palpable. It is important, I believe, in examining the thyroid always to have the patient stand, always to have the head erect, not hyperextended—a position which tenses the muscles—not bent so that the gland dips below the clavicles, but with the head in a natural position. Then the thyroid is readily palpable on deglutition.

The patient also has a fine tremor, which is hardly visible but is easily palpable. You can often feel the tremor better than you can see it. The hands are moist and warm, and there is a persistent tachycardia and a forceful apical impulse—again an expression of the attempt of the circulatory system to compensate for the hypermetabolism.

Here we have objective evidence of early hyperthyroidism, so early that the patient was not aware of it, so early that the thyroid itself is barely palpable.

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Figure 5. Lateral x-ray view of middle lobe atelectasis.

step in a vicious circle has become established. Obstruction to the bronchus inevitably leads to infection and the infection perpetuates the lymphadenitis.

The impression is not to be left that the stenosis results purely from the pressure of lymph nodes. The bronchial stenosis may not be due entirely to pressure by enlarged glands but may in part be caused by spread of infection through the bronchial wall from the glands with resultant edema and even, at times, stricture.

It is pertinent to emphasize that in the investigation of these cases all lobes should be investigated since it is possible for the original primary lesion to have been located in the

lower or upper lobe on the right side and the middle lobe to have become involved more or less as an innocent bystander because of its strategic position.

The treatment, of course, is obvious and has been simple. In all twelve cases a middle lobe lobectomy by the individual ligation technic was carried out. All patients made perfectly uneventful recoveries and have remained free of symptoms since operation.

REFERENCES

1. BROCK, R. C., CANN, R. J., and DICKINSON, J. R.: *Guy's Hosp. Rep.* 87:295, 1937.
2. BROCK, R. C.: *The Anatomy of the Bronchial Tree*. Oxford Medical Publications, London, 1946.
3. ZDANSKY, E.: *Wien. klin. Wchnschr.* 58:197, 1946.

tion of the basal metabolic rate indicated that a residual hyperthyroidism was present. In the presence of a low-grade postoperative residual hyperthyroidism, cures of hyperthyroidism were rarely seen. These are the patients in whom the hyperthyroidism recurs, usually within a year of operation.

Why do not all patients have a recurrence of their hyperthyroidism after thyroidectomy? That is a thing we do not understand, because the mechanism that produced the original hypertrophy and hyperplasia of the thyroid is still present after subtotal removal of the thyroid gland. Inasmuch as that mechanism is still present, why does it not induce the remnants of the thyroid again to undergo hypertrophy and hyperplasia and again to produce hyperthyroidism in that individual? The only answer which we have is speculation that an adequate thyroidectomy in which the metabolic rate is driven to subnormal levels, to -10 , -15 per cent, and maintained there for a period of time, breaks some vicious circle in the course of the disease. The hyperthyroidism then goes into a remission just as it occasionally goes into a spontaneous remission without any form of therapy. An adequate thyroidectomy, then, will cure the disease. Inadequate thyroidectomy or iodine therapy will not cure the disease.

I make this analogy because it is so important for one to realize it when using the antithyroid drugs. Propyl thiouracil, particularly, is a weak antithyroid drug as compared with the parent drug, thiouracil, and only produces an iodine block, as Dr. Astwood has found, that is to say, a block in the uptake of radioactive iodine for four hours after an adequate dose, whereas thiouracil produces a block for twenty-four hours.

IN OTHER words, the block in formation of thyroid hormone after an effective dose of propyl thiouracil is a short block, and that is why some patients are found to be resistant to this drug. In some patients, in spite of adequate dosage, the metabolism falls to only $+10$ or $+15$ per cent. So in those patients whose

metabolism is not completely controlled by propyl thiouracil, regardless of how long one continues the treatment, there is still some residual hyperthyroidism, and the situation is exactly comparable to that of the patients who were treated with iodine and that of the patients who had an inadequate thyroidectomy with a low-grade residual hyperthyroidism.

Recurrences will be the rule in those patients inadequately treated with propyl thiouracil. It may be that propyl thiouracil will not be the ultimate answer for all patients; it may be that methyl thiouracil or some other derivative of thiouracil will be more effective in the long run in causing a universal and complete control, driving the metabolism to zero or even to subnormal levels.

In the meantime, however, the majority of patients do respond in a satisfactory manner to treatment with propyl thiouracil. Most of them can reach zero or less if adequate doses of 300 mg. daily are given. It should be remembered, however, that the dose should be distributed as widely as possible through the day because of the short action of the block in this drug. It should be given at least four times daily, after every meal, and at bed time. It should not be given in just morning and night dosages, for then the thyroid will make a complete recovery from the block before the next dose is given.

In the treatment with antithyroid drugs we are aiming, not merely to relieve the patient's symptoms, or to reduce the metabolism to the upper limits of normal, but to control the disease completely; we are aiming to block the vicious circle which we presume causes this disease and to accomplish exactly the same thing as an anatomic thyroidectomy does, namely, a physiologic thyroidectomy, bringing the patient to a normal thyroid or a hypothyroid state. If we fail to accomplish this our chances of accomplishing cure by medical means are reduced to insignificance.

I think it is safe to say, therefore, that at the present time the responsibility for the treatment of hyperthyroidism has shifted. It used to be the responsibility of the surgeon to perform an adequate thyroidectomy and to prevent re-



GEORGE CRILE, JR.

Now the problem of treatment of this condition comes up. Here is a patient who is not aware of illness. She would not willingly rush to the surgeon to have the thyroid removed at this time. This, in my opinion (and I am sure in her opinion), is an ideal case for the medical treatment of hyperthyroidism. If this medical treatment is carried out properly, fully, and over a long enough period of time, there are good prospects that this patient may obtain a long-standing, if not a permanent, remission by medical means alone and that surgery will not be necessary.

I do not believe it would be fair to the patient to tell her that surgery is necessary or will eventually be necessary and prepare her either with iodine or with an antithyroid drug and perform a thyroidectomy. If this patient is prepared with an antithyroid drug and her metabolism reduced to normal, it would be better

to continue the treatment for a little longer and see if she will not spontaneously enter a long-standing or permanent remission.

Also, it is not fair in such a patient to state that surgery will not be necessary. She has just been started on propyl thiouracil. We do not yet know how her hyperthyroidism is going to react to this drug. It is entirely possible that the gland may enlarge rapidly under treatment, as is sometimes the case, and under such circumstances thyroidectomy does become necessary. Therefore, the best way to handle this particular problem is to say, "You have a disease which appears at the present time to be well adapted to medical treatment. We cannot promise you that surgery is not eventually going to be necessary, but we believe that medical treatment is worth a trial in that it will give you probably better than a 50-50 chance of entering a long-standing if not a permanent remission."

What are we going to attempt to do? What is the rationale of the medical treatment, or of surgical treatment for that matter? We know too well from our experience with iodine that it does not commonly cure hyperthyroidism. Iodine alleviates the symptoms temporarily.

We know that if we give iodine to a patient with a $+75$ basal metabolism who has not had iodine before, the metabolism usually will fall to a little less than half the previous level. Between 25 and 50 the metabolism will form a plateau. We also know that iodine, no matter how long it is given nor in what doses, will rarely drive the metabolic rate to lower levels. There is a persistent residual hyperthyroidism present in these cases; as long as that residual hyperthyroidism is present, the hyperthyroidism becomes worse on withdrawal of iodine. The patient is again in as severe a state as she was in the beginning.

What happens with thyroidectomy? In the early days of thyroidectomy the operation was often incomplete; not enough gland was removed, and the metabolism would fall perhaps to $+10$, perhaps to $+15$ per cent, and stay at that level. The patient was gratified. She felt much better, she gained weight, and symptoms were relieved. However, critical examination and, most important of all, accurate determina-

tion of the basal metabolic rate indicated that a residual hyperthyroidism was present. In the presence of a low-grade postoperative residual hyperthyroidism, cures of hyperthyroidism were rarely seen. These are the patients in whom the hyperthyroidism recurs, usually within a year of operation.

Why do not all patients have a recurrence of their hyperthyroidism after thyroidectomy? That is a thing we do not understand, because the mechanism that produced the original hypertrophy and hyperplasia of the thyroid is still present after subtotal removal of the thyroid gland. Inasmuch as that mechanism is still present, why does it not induce the remnants of the thyroid again to undergo hypertrophy and hyperplasia and again to produce hyperthyroidism in that individual? The only answer which we have is speculation that an adequate thyroidectomy in which the metabolic rate is driven to subnormal levels, to -10 , -15 per cent, and maintained there for a period of time, breaks some vicious circle in the course of the disease. The hyperthyroidism then goes into a remission just as it occasionally goes into a spontaneous remission without any form of therapy. An adequate thyroidectomy, then, will cure the disease. Inadequate thyroidectomy or iodine therapy will not cure the disease.

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Figure 1. Small diffuse goiter with hyperthyroidism suitable for definitive treatment with propyl thiouracil.

currences of hyperthyroidism. Today the challenge is with the internist. The internist is challenged not only to reduce the metabolism to zero or less, but he must maintain it at that level over a long period—sometimes a year. The exact length of time needed to produce a long-standing or permanent remission is not known.

It may be that more intense treatment carried out over a shorter period of time will be as effective as maintaining a normal thyroid activity or slightly hypothyroid state for a longer period of time. We know that the metabolism must be driven down and must be maintained at those levels if a long-standing remission is to be accomplished. We also know that if this is done, the incidence of long-standing remissions will be at least 50 per cent—I believe much

closer to 75 per cent—in those patients who can be carried through this length of time.

A CERTAIN percentage of patients are resistant to treatment with propyl thiouracil. That is why when one first sees a patient one cannot state, "We can cure you medically," because one does not know what the reaction to the drug is going to be. Some patients will respond slowly, some will respond incompletely; in some of them, extremely high doses will be required, and the resistant patients will usually be the ones who will develop recurrences as soon as the drug is withdrawn. Finally, the gland may enlarge under treatment. This is a bad sign. In those patients whose glands enlarge, the recurrences usually take place promptly and one has to discontinue the medication because of the progressive enlargement.

Therefore, in those patients who do not respond satisfactorily to an empiric trial (and they constitute at least 25 per cent of the patients with Graves' disease) the internist should not force the issue; he should not attempt, regardless of the type of response, to make the patient go on with medical treatment when it becomes clear that surgery would give a more prompt and definitive answer to the problem.

At the present time, therefore, our plan of treatment is as follows. The patients are divided roughly into four groups:

(1) Those patients with Graves' disease with goiters of moderate size. If the gland is of small or moderate size, which is the case in 85 per cent of the patients with Graves' disease, then I think it is worth a trial at medical treatment, provided one can have the full cooperation of an intelligent patient who will do exactly as one says over as long a period as recommended. However, if the goiter is large enough to be visibly deforming, that is to say, a big diffuse goiter, I believe it is foolish to try to treat it indefinitely by medical means. These often enlarge further under treatment and it is better to advise preparation with an antithyroid drug and thyroidectomy (Figure 1).

(2) Those with large goiters, either adenomatous or diffuse. These patients can be pre-



Figure 2. Large diffuse goiter with hyperthyroidism suitable for preparation with propyl thiouracil and thyroidectomy.



Figure 3. Nodular goiter with severe hyperthyroidism suitable for preparation with propyl thiouracil and thyroidectomy.

pared with an antithyroid drug and operated upon (Figures 2 and 3).

(3) Those who have a mild hyperthyroidism and young patients who are good surgical risks. These can be prepared with iodine and the thyroid can be removed (Figure 4).

(4) Finally there is a group of patients who have either mild or severe hyperthyroidism but whose age, debility, or complicating diseases shorten the life expectancy. In these cases it is unwise to advise surgery when the disease can be handled indefinitely and satisfactorily by medical means (Figures 5 and 6).

Figure 1 shows an individual who has a mild hyperthyroidism with a basal metabolic rate of +30 per cent, a young woman who has a small goiter which is barely palpable. This type of

patient is ideally adapted for a definitive treatment with one of the antithyroid drugs, and the best available at the present time appears to be propyl thiouracil.

THE TYPE of patient in Figure 2 falls into Group 2, in that she has an exophthalmic goiter, that is to say, Graves' disease, but it is a large diffuse goiter, plainly visible, and is large enough to be of cosmetic importance. There is little chance that permanent control of the hyperthyroidism and of the goiter will be effected by the use of an antithyroid drug. Preparation with one of the antithyroid drugs, followed by thyroidectomy, would be indicated in her case.



Figure 4. Large adenomatous goiter with low grade hyperthyroidism suitable for preparation with iodine and thyroidectomy.

A large nodular goiter with severe hyperthyroidism will be observed in Figure 3. Operation in such a patient, whose basal metabolic rate is over $+60$ per cent, would entail considerable hazard. It would not be correct to prepare her with iodine and operate on her, because the iodine would not effect a significant reduction in her basal metabolic rate or in the severity of her hyperthyroidism. This is the type of patient who should be prepared with an antithyroid drug and then operated upon. It may take a long time for this patient's hyperthyroidism to come under control.

In the presence of large adenomatous goiters, it may take months for the hyperthyroidism to

be controlled with antithyroid drugs. Propyl thiouracil may fail completely, and it may be necessary to resort to methyl thiouracil or even to the parent drug, thiouracil, in spite of its toxicity, in order to subdue the hyperthyroidism associated with this huge nodular goiter. It would not be correct, however, to assume the risk of operation in aged patients who have cardiac decompensation and large goiters with severe hyperthyroidism without first completely controlling the hyperthyroidism. This principle of not operating on patients with hyperthyroidism which is not controlled has resulted in an astonishing reduction of mortality in thyroid surgery. (Figure 4.)

The patient in Figure 3 presents a little different problem, in that she has an adenoma in the thyroid which would be classified as a solitary adenoma of the thyroid. It involves only the right lobe; it is firm and is of a different consistency from the rest of the gland. The other side is normal. She has a severe hyperthyroidism, however, which makes it unlikely that this tumor in the thyroid is malignant. Hyperthyroidism and malignancy are not often associated in the same gland. Nevertheless, she has a solitary, firm, discrete adenoma of the thyroid. The presence of malignancy cannot be excluded, and it is best in these cases to prepare the patients with an antithyroid drug and remove the thyroid. After it is out the patient is always grateful because she is rid of the tumor which is large enough to be of cosmetic importance to her.

The patient in Figure 5 is old; she is a poor risk; her life expectancy is short. It makes little difference whether you advise surgery or medical treatment in this instance. This patient can just as well be treated indefinitely with propyl thiouracil. She has pernicious organic heart disease and requires medical treatment intermittently. It is not necessary to advise thyroidectomy unless the patient proves resistant to the drug.

A patient who has had three previous thyroidectomies, x-ray to the point of skin tolerance (you can see the pigmentation from the x-ray) and still has a basal rate of $+65$ per cent



Figure 5. Hyperthyroidism in an elderly patient with organic heart disease and a relatively short life expectancy. Indefinite treatment with propyl thiouracil justified.



Figure 6. Hyperthyroidism recurrent after two thyroidectomies and x-ray therapy to tolerance. Indefinite treatment with propyl thiouracil justified.

is pictured in Figure 6. In this type of patient the morbidity of thyroid surgery, the possibility of producing parathyroid tetany or recurrent laryngeal nerve injury, is too high to justify operation. Indefinite treatment with propyl thiouracil or the use of radioactive iodine is clearly indicated.

SUBACUTE thyroiditis can be confused with hyperthyroidism, and these patients should not be operated upon because it will subside spontaneously in time. It may respond to use of the antithyroid drugs, and x-ray treatment in small doses will specifically relieve the symp-

toms within two weeks of the onset of treatment. Tenderness over the thyroid and the systemic symptoms suggestive of hyperthyroidism characterize this disease.

Hyperthyroidism in children may be of a resistant type but a trial on medical treatment may be worthwhile. On the other hand, one cannot guarantee that medical treatment is going to effect a cure because hyperthyroidism occurring in children is a severe form of the disease. Often the thyroid will enlarge and the hyperthyroidism will not be well controlled. I think it is worth a trial, but we cannot guarantee that it will work.

In conclusion, therefore, I believe that a broad

analogy can be drawn between the treatment of peptic ulcer and the treatment of hyperthyroidism. When the patient first comes to you with a peptic ulcer you do not say, "You must have a surgical operation." You do not say, either, that this certainly can be cured by medical treatment. Certain types of ulcer, obstructing ulcer, ulcer bleeding uncontrollably in spite of very good medical treatment, you know are going to require surgery. There are certain types of goiter that you know are going to require surgery. What you tell a patient when he comes in either with Graves' disease or with ulcer is "Let's give this a therapeutic trial on medical treatment; let's not make up our minds definitely until we see how this disease of yours responds to medical treatment. After that it is time to decide when surgery is indicated."

Patients with simple goiter should not be treated with the antithyroid drugs. The antithyroid drugs are goitrogens. In animals, goiter is routinely produced by the administration of these drugs. If an antithyroid drug were given to the patient here probably nothing would happen to the size of the gland, but if anything did, it would be enlargement of the thyroid.

What are the chances of malignancy occurring in such a gland? We know that many statistics have been published recently, and they are mainly surveys of autopsy material from large hospitals which show a low incidence of carcinoma of the thyroid, or figures compiled by surgeons which show an extraordinarily high incidence of carcinoma of the thyroid.

OF RECENT statistical surveys, one of the most striking was by Cole who showed an incidence of malignancy of the thyroid in solitary adenomas of the thyroid as high as 24 per cent. This seemed incredible to me, and I analyzed our figures and my own experience with solitary adenomas of the thyroid. I was surprised to find that if I included all malignancies of the thyroid (most of them are solitary tumors of the thyroid) and threw them into the group of solitary adenomas, the incidence of malignancy in solitary tumors was as high as 26 per cent.

But there is something wrong with these figures. You know that in your practice 26 per cent of the patients who walk into your office with solitary tumors in the thyroid do not have cancer of the thyroid.

In order to try to interpret this I surveyed the incidence of goiter in patients coming routinely to the Cleveland Clinic, which, of course, is in and on the outskirts of regions of endemic goiter. The incidence of adenomatous goiter occurring in patients not coming in and presenting the complaint of goiter but coming in with chief complaints referable to other systems was 4 per cent. Approximately a fourth of these could be considered to be more or less solitary adenomas.

This means that over the same period of time that this survey was conducted, in which a certain number of carcinomas of the thyroid were found, there were about 1,300 patients who came to the clinic in whom operation was not advised at all. These patients went home and as far as we know no further difficulty was experienced with the adenomatous goiter. So the figures can be interpreted in various ways. I could say, and be statistically quite correct, that when a patient comes to my office with an adenomatous goiter with a single nodule in the thyroid, there is one chance in four that it is a cancer. Because every cancer of the thyroid cannot be diagnosed, I could tell her that there is a 5 per cent chance that the lump in the neck is a cancer.

That is an alarming figure. When a patient has a lump in her neck and one can only say that there is a 5 per cent chance that it might be a carcinoma, she will be alarmed and want to have it removed. On the other hand, I could say just as accurately, on the basis of the overall experience of the clinic, including the cases which were not operated on, that there was only one chance in 1,300 that the solitary tumor was a cancer of the thyroid. So it is a matter of the presentation of the statistics.

I do not believe that there are any adequate statistics available to date which indicate the true incidence of carcinoma in adenomas of the thyroid. That would be a difficult study to

make. Until we know what the actual incidence is, I think we are forced to disregard statistical surveys completely, whether they come from autopsy studies in hospitals or from the surgeon's laboratory. I think we must rely on clinical judgment and consider any tumor which is firm, discrete, or enlarging to be possibly malignant, and not say that every soft little involutary nodule in the thyroid has an 8 per cent chance of being cancer.

Thousands of these patients are not even aware of lumps in their necks. Thousands of

them have been told by their physicians, "There is no chance of the lump's being malignant." In thousands more the surgeon had advised against operation. All these have been disregarded in the surveys made by surgeons but should be included if the statistics are to be significant. Until we know more let us advise surgery in those patients in whom the goiters are large enough to be of cosmetic importance and those in whom clinical experience suggests the possibility of malignancy.



DAS NARRENSCHNEIDEN

Franz Hals, the Younger

Ligation of Persistent Ductus Arteriosus

JAMES L. MUDD*

ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

THE ductus arteriosus is a normal structure which short-circuits the blood from the pulmonary artery back into the systemic circulation when the child is carried in utero. It normally atrophies and leaves as a remnant the ligamentum arteriosus. Christie, in a series of autopsies, found that the ductus normally disappears within the first three months of life and that 98.8 per cent are closed within the first year, leaving an incidence of 1.2 per cent which exist after one year of life.

Maud Abbott, in a series of 92 fatal cases of ductus arteriosus, found that the cause of death in about 50 per cent was congestive heart failure and that, interestingly enough, 30 per cent died of streptococcus viridans infection.

The clinical features of ductus arteriosus vary. Most striking is the machinery-like murmur which is heard over the entire precordium and is best heard in the second interspace on the left. This is a continuous machinery-like murmur and there is usually a low diastolic pressure.

Many investigators have pointed out that children with persistent ductus arteriosus are

undernourished, but though many of them are, that is not always true. In fact some of my patients have been obese.

In 1907, Dr. John C. Monroe of Boston, in an address before the Philadelphia Academy of Medicine, described a child who seemed perfectly normal, but on straining would faint and, on several occasions, was apparently dead. The child eventually died, and on autopsy the only anomaly that could be found was a persistent ductus arteriosus. Monroe called on the pediatricians present to make the diagnosis of persistent ductus arteriosus and on the surgeons to attempt obliteration of the ductus, but it was not until May 1938 that anyone attempted the operation. Monroe worked out a technic of splitting the sternum as an approach to the ductus.

The attempt of Graybiel and Streater in a patient with a persistent ductus, who incidentally had streptococcus viridans, was made through the approach suggested by Monroe of splitting the sternum. Their patient survived the operation but died four days later, supposedly of gastric dilatation.

In August of 1938, Robert Gross of Boston first successfully ligated ductus arteriosus. Gross used a new approach that he had worked out, a transpleural approach.

*Assistant Professor of Surgery, St. Louis University School of Medicine, St. Louis.

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At the meeting of the American Association for Thoracic Surgery in Cleveland in July 1940, Dr. Arthur Turoff, of New York, reported four very interesting cases. He had four patients with a persistent ductus complicated by streptococcus viridans. His first patient survived the operation and was cured of his streptococcus viridans. The next two patients, as I recall, died of uncontrollable hemorrhage, and the fourth patient eventually died of streptococcus viridans.

Interestingly enough, Dr. Turoff's first patient survived the operation and was cured of streptococcus viridans. Why the patient should be cured of viridans we do not know. There have been some interesting speculations, but no one has proved them. This, of course, was in the days before penicillin. There have been some reported cases, as you all know, of the cure of streptococcus viridans by employing massive doses of penicillin.

IN NOVEMBER of 1940 we had occasion to operate on our first ductus. This was in a child at the City Hospital. She was overweight, if anything. She had had diphtheria and was sent to the isolation hospital here. It had been known that she had a congenital lesion of some sort almost from the time that she was born. When she came into the isolation hospital with diphtheria the diagnosis of a persistent ductus was made. Because of the reports of Maud Abbott that the average age of death in patients with persistent ductus was 24 years and that they died of congestive heart failure, and because diphtheria is a noted damager of heart muscle, we suggested to the parents of this child that the ductus be ligated. The attempt was successful and the child left the hospital shortly after the operation.

In December 1940, a 14-year-old boy was admitted to St. Mary's Hospital with a low-grade fever, a persistent murmur, and a low diastolic pressure. The blood cultures were positive for streptococcus viridans. With the one successful report of Dr. Turoff of the cure of streptococcus viridans by ligation, we suggested

to the parents of this boy that an attempt be made to close the ductus. The boy had as many as 800 colonies per cubic centimeter. The day before he was operated on he had 500 colonies. The day after his operation he had 3 colonies. All subsequent cultures have been negative.

Immediately after ligation the murmur and the thrill disappeared and the boy made an uneventful recovery except for a pleural effusion. This was early in our experience with the use of sulfa drugs, and because he developed an effusion we put him on sulfa drugs. His temperature went up; he had a beginning murmur, and I thought that we were in for failure. He developed a rash, and that put us on the right track; we discontinued his sulfa drugs, and, of course, his temperature and the rash disappeared, as did the murmur.

That was seven years ago. The boy is perfectly well, and the last I heard from him he had finished high school and was a candidate for the Army. I advised against military service for him, however, but I think he might even have gone through that.

We have had occasion to ligate 8 patients with a persistent ductus complicated by streptococcus viridans. Seven of them have been cured of their viridans. One of them died. The one that died I think is of interest because whenever we see a patient with a ductus the question always arises, "Is the ductus a safety valve for some other cardiac lesion and should it be ligated?" I know of no way to answer that question except to say that the incidence of other congenital lesions should not be any higher in the group with a persistent ductus than it is in normal individuals. If the patient has a machinery-like murmur of the second interspace with a low diastolic pressure, I think you are justified in exploring it.

We usually put a tourniquet around the ductus and clamp it off to see what happens to the circulation, to the murmur, and to the blood pressure. If we leave the tourniquet on for any length of time and nothing untoward happens, then we go ahead and ligate.

In the case of a 9-year-old boy who had repeated positive blood cultures for viridans, we

ligated his ductus, but his murmur did not disappear. His cultures were negative for a few days and then became positive. Someone in New York was using massive doses of the sulfa drugs for viridans. The boy had an aunt who was a physician in New York and they requested that he be transferred to New York for treatment with sulfa drugs. Since I certainly had nothing more to offer (I had ligated his ductus and his viridans continued), the boy left the hospital about a month after ligation. He still had a murmur; he still had his viridans. They arrived in New York Wednesday and the boy suddenly died on Sunday before any treatment had been given.

I was unable to get a copy of the protocol, but the parents told me that other congenital lesions were found at autopsy.

OUR YOUNGEST patient was 3 years old, and the oldest was 42. We feel that the ideal age for the patient to undergo the operation is 4 or 5 years. Three is a little young; it is a little more technically difficult to do the operation at that age. We feel that these patients should be ligated before they go to school. I feel that every young child, at least, who has a persistent ductus should have it obliterated. The mortality rate from the operation is very low; the incidence of streptococcus viridans is high, and the incidence of congestive heart failure is high. I feel that it is much less of a risk to the patient to have his ductus ligated than it is to let him go on through life with it. I know that every once in a while you will see an adult who has a very large ductus and apparently had no trouble throughout life.

I feel that all children under 12 who have a persistent ductus should have it obliterated. Adults certainly should have it ligated if it is

infected; they should certainly have it ligated if they show signs of congestive failure or if they show cardiac enlargement, which many do.

When performing the operation, the best landmarks are the phrenic and the vagus nerves. The incision in the mediastinal pleura is made between the phrenic and the vagus nerves, and if you follow the vagus down you find the recurrent tucked in right at the ductus, and the recurrent is the best landmark for the ductus. In the female the incision is usually made beneath the breast and the breast is retracted upward so that when the scar heals it will be hidden by the breast and will be unnoticeable.

In some of our operations we have removed a rib because it makes the closure a little easier. It is not necessary for exposure, however.

There is frequently an intercostal vein in the line of incision which we pick up and ligate. It is in the separation of the posterior wall of the ductus that we get into difficulties. If hemorrhage is going to occur, it usually occurs when we are separating the posterior wall.

Recently there has been somewhat of a controversy as to whether the ductus should be simply ligated or whether it should be severed and the two ends ligated separately. There have been some reports of recanalization of the ductus, but I think the use of the tourniquet is rather important. By clamping down the rather broad base of the tourniquet, I think that we damage the intima sufficiently and if we put on a tight suture there will be less tendency to recanalization. I have operated on 16 of these patients, none of whom have recanalized. In my cases the vessel was not severed; it was simply ligated.

Some of the untoward effects of ligation have been failure to find the ductus, ligation of the wrong vessel, infection, and hemorrhage.

Diagnosis and Management of Regional Enteritis

CHARLES B. PUESTOW*

UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE, CHICAGO

ULCERATIVE lesions of the bowel have been reported in medical literature as far back as 1806 and subsequent reports are voluminous. However, it was not until 1932 that a definite clinical entity termed "regional ileitis" was reported by Crohn, Ginsberg, and Oppenheimer. They defined the disease as "a chronic, nonspecific, granulomatous, inflammatory process occupying for the most part the terminal segment of the ileum, and characterized by diarrhea, fever, obstructive phenomena, and often by fistulous tracts." These authors described the symptomatology of the disease and their concepts of the pathology, etiology, and treatment.

Many names have been given to this disease. The interest stimulated by Crohn and his co-workers produced other reports on inflammatory lesions of the bowel. It soon was recognized that the granulomatous lesions were not limited to the terminal ileum but could involve any portion of the small intestine and occasionally areas of the colon. Because any portion of the bowel may be involved, and because multiple lesions frequently are found with normal segments of

bowel between, the term "regional enteritis" has been commonly adopted. After a careful review of the literature, Shapiro concluded that the term "nonspecific inflammatory granuloma" followed by the designation of the portion of the bowel involved would be an appropriate terminology for this disease. However, a more suitable name may suggest itself when the true etiology of this disease is better understood.

ETIOLOGY

The etiology of regional enteritis is unknown. As is true in other conditions which are not clearly understood, many theories have been advanced as to the cause of this disease. It is evidently an infectious process. Whether or not the infection is secondary to some other factor such as trauma is difficult to determine. Originally, the disease was thought to be associated with appendicitis, the infection spreading from the appendix to the terminal ileum. However, in many cases of regional enteritis the appendix is not diseased. Because of the marked involvement of the mesenteric lymph nodes, this disease has been attributed to lymphatic block. The lymphatic involvement is more likely to be secondary to the infection that is associated with

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extensive ulceration and inflammation within the bowel.

Bacillary dysentery was believed to be related to this disease. Other organisms considered as etiologic factors were the tubercle bacillus, various gram-positive cocci, and bacteria of all types as well as bacterial toxins. A theory of relationship to lymphogranuloma inguinale has been advanced. A clinical similarity to certain virus diseases and the profusion of eosinophiles in regional enteritis have suggested the possibility of a virus etiology. Achylia gastrica has been considered as a related condition because of the absence of disinfecting power of hydrochloric acid and gastric juice. However, many patients with normal or increased gastric acids develop regional enteritis.

Many other factors have been suggested as being responsible for or contributory to this disease. They include allergy, interference with the blood supply, the presence of foreign bodies in the bowel, trauma, and heredity. There is reason to believe that overdistention of the bowel,

to a degree of damage to the mucosa sufficient to permit the intestinal flora to penetrate the bowel wall, may be followed by ulcerative lesions.

SYMPTOMATOLOGY

THE SIGNS and symptoms of regional enteritis vary with duration of the disease and the stage in which the patient is first seen. Although all patients do not run identical courses, the description of four stages by Crohn will apply to a high percentage of individuals suffering with this condition. These stages are as follows:

(1) Acute or surgical abdomen. The disease often begins with acute manifestations suggestive of appendicitis. This is evidenced by the fact that approximately 50 per cent of patients in the early stages of regional enteritis are operated for appendicitis. They present signs and symptoms of peritoneal irritation most frequently in the right lower quadrant. Fever, leukocytosis, tenderness, muscle spasm, and diarrhea often accompany the onset of the disease. Not all patients have an acute episode at the onset. Many have a slow, progressive development of symptoms.

(2) Symptoms of ulcerative enteritis. In this stage of the disease the patient complains of colicky abdominal pain. A low grade diarrhea with blood and mucus in the stool associated with a slight elevation of temperature, progressive weight loss, anemia, and weakness are common. Tenesmus is a rare complaint. Low abdominal tenderness frequently is present and a palpable mass may be noted in the right lower quadrant or in the lower abdomen. The presence of a mass is indicative of mesenteric involvement.

(3) This is a stage of chronic incomplete intestinal obstruction and is brought about by gradual stenosis of the bowel. In some patients this is the first manifestation of the disease. Symptoms frequently consist of abdominal cramps, borborygmus, visible peristalsis, distention, and occasional vomiting. Constipation may replace diarrhea. The general debility of the patient is progressive. A palpable mass in the lower abdomen usually is present.



Figures 1 and 2. The string sign of Kantor as demonstrated by barium enema.

(4) This is a stage of chronic fistula formation as well as other complications. A variety of complications including obstruction, perforation, development of abscesses, and the establishment of fistulas may result. Internal fistulas between various loops of bowel, between the bowel and other hollow viscera, or between the bowel and the abdominal wall, perineum, or pelvic organs may occur. Perirectal abscesses and fistulas secondary to regional enteritis have been reported in 15 per cent of cases.

In all stages of the disease, blood is present in the stools and produces a high incidence of secondary anemia. Occasionally, massive hemorrhage occurs.

DIAGNOSIS

DIAGNOSIS of regional enteritis can be made clinically, radiologically, and surgically. In the acute stage it may be made only by exploratory laparotomy. In the subacute and chronic stages it may be made by x-ray examination alone when the essential roentgen finding is a stenosis of the terminal ileum resulting

in the typical "string sign" of Kantor. This sign can be demonstrated in most cases by barium enema alone as a result of the reflux of the barium through the ileocecal valve. (Figures 1 and 2.)

Occasionally, careful studies of the small bowel are necessary. This is accomplished by giving the patient swallows of thin barium and making x-ray studies of the small bowel at hourly intervals for six to fourteen hours. (Figure 3.) This technic frequently will visualize multiple areas of constriction and dilatation in the course of the small bowel. (Figures 4 and 5.) Other roentgen findings are constant non-visualization of the involved segment in some cases, dilatation of the intestine proximal to the involved segment, deformity of the cecum, and displacement of the normal intestine by a mass in the right lower quadrant. The absence of a normal barium shadow in the proximal colon was described by Stierlin in 1911 and this has since been known as Stierlin's sign. It was considered indicative of tuberculosis but any ulcerating granuloma of the ileocecal region can have a similar roentgen appearance.

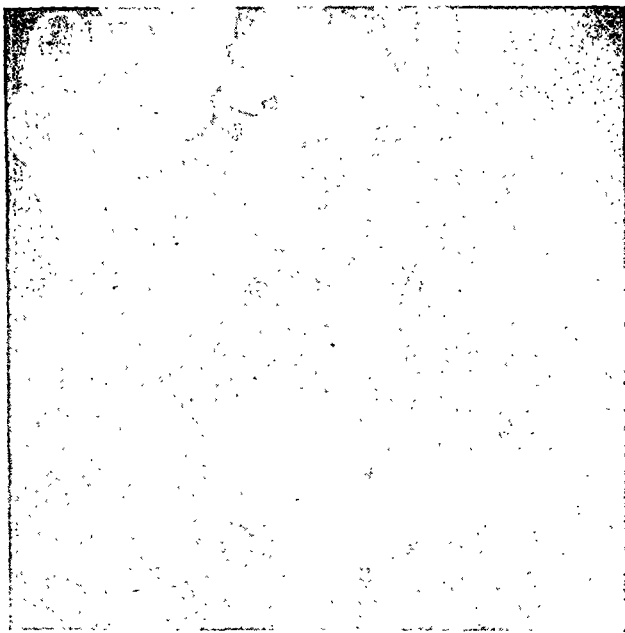


Figure 3. Regional enteritis of terminal ileum demonstrated by thin barium given by mouth.

DIFFERENTIAL DIAGNOSIS

The three most important diseases to be differentiated from regional enteritis are appendicitis, tuberculous enteritis, and ulcerative colitis. Others are diverticulitis, amebiasis, sarcomatosis of the small intestine, nontropical sprue, Hodgkin's disease, and foreign bodies.

The differential diagnosis between regional enteritis and appendicitis already has been discussed. The signs and symptoms may be identical except for the presence of diarrhea in the former. In regional enteritis the white blood cell count is usually higher than that found in the typical case of appendicitis, reaching as high as 20,000 to 25,000. The elevation of temperature in the acute stage usually is higher than that found in appendicitis. In about one-half of the cases the differential diagnosis can be made only at operation. In the subacute and chronic stages the differential diagnosis is more obvious because of the signs and symptoms of partial bowel obstruction, the duration of the disease, and the presence of weakness and loss of weight.

In nearly every case of tuberculous enteritis,

pulmonary tuberculosis is present. The case in which evidence of pulmonary tuberculosis is lacking is rare. Tuberculous enteritis seldom results in partial bowel obstruction and in most cases its presence is manifested only by diarrhea. X-ray examination of the gastrointestinal tract will not differentiate between the two conditions, nor will the gross pathology noted at surgery. Microscopically, one will find the typical tubercle in tuberculous enteritis.

OCCASIONAL association of regional enteritis and nonspecific ulcerative colitis makes differentiation difficult. A common pathogenesis may be found for the two conditions. In most cases, however, one can distinguish between the two by proctoscopic examination and barium enema. In the uncomplicated case of regional enteritis, proctoscopic examination will reveal a normal colon, whereas the typical picture of ulcerative colitis will be observed in the latter condition. There is no small bowel pathology in the usual case of ulcerative colitis as shown on roentgen examination. The diagnosis of diverticulitis also can be made on roentgen examination.

Amebiasis may be diagnosed by examination of the stool and proctoscopy, but x-ray examination may be of little diagnostic value.

Sarcomatosis of the small intestine is rare but occurs frequently enough to warrant consideration. The differentiation is made by exploratory laparotomy and histopathologic studies.

Nontropical sprue is distinguished by the appearance of the stool. Hodgkin's disease is characterized by systemic manifestations, presence of lesions extrinsic to the small bowel, and by its microscopic appearance.

PATHOLOGY

At operation in the acute stage the terminal ileum or involved segment of small intestine may reveal only an edematous, reddened, granular serosa. Usually there is a little serosanguinous fluid within the peritoneal cavity.

Later there will be numerous stringy adhe-



Figures 4 and 5. Multiple areas of constriction demonstrated by barium studies.

sions resulting in a matting together of several loops of small intestine. The appendix or cecum may be involved in this process. There is always a striking mesenteric lymphadenopathy and thickening of the mesentery. (Figure 6.)

When more than one segment of bowel is involved the intervening intestine and mesentery usually appear normal. This situation has given rise to the term "skip areas." In the chronic stage, scar tissue may cause partial or acute bowel obstruction with dilatation of the proximal bowel. The diseased bowel may be greatly thickened and "garden hose" in character. The mucosa presents small ulcerations along the mesenteric border and much folding and overgrowth as a result of the contracting scar tissue. This markedly diminishes the lumen and accounts for the characteristic x-ray appearance.

Microscopically the picture of regional enteritis is one of chronic inflammation and chronic lymphedema. There is marked fibrosis and thickening of submucosal and mucosal layers. (Figure 7.) The entire structure of the bowel wall may show a mononuclear infiltration with a preponderance of these cells in the mu-



Figure 6. Photograph of segment of small intestine showing ulceration of mucosa, thickening of the bowel wall, edema of the mesentery and lymphadenopathy characteristic of regional enteritis.

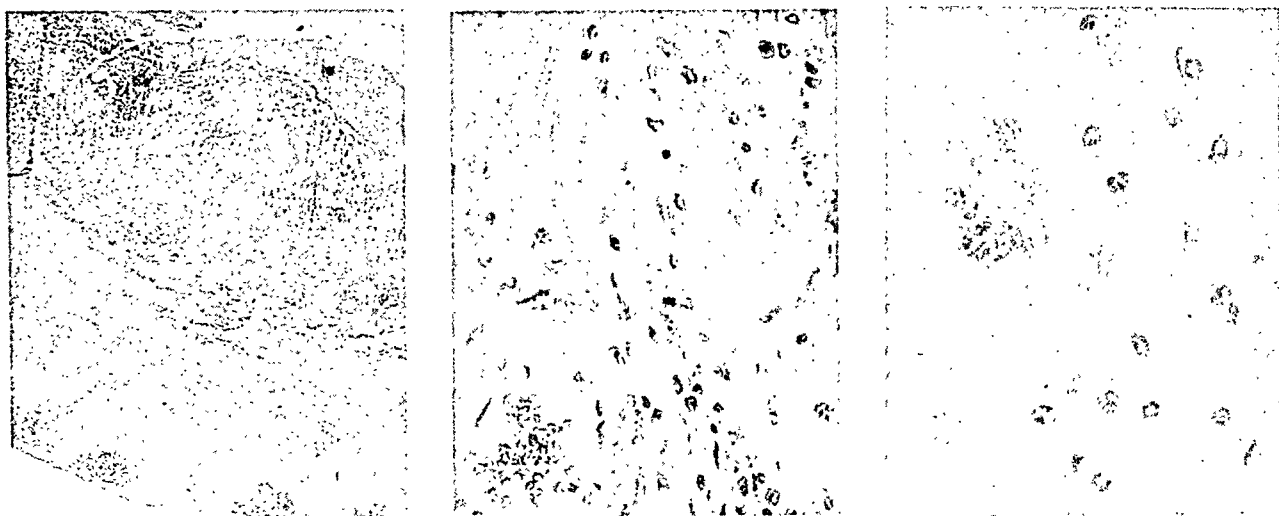


Figure 7 (left). Cross section of bowel wall in regional enteritis showing marked thickening. Figure 8 (center). Histologic picture of bowel wall in regional enteritis showing mononuclear infiltration. Figure 9 (right). Giant cells seen in regional enteritis.

cosal layer. (Figure 8.) Giant cells are commonly seen and have been responsible for the erroneous assumption that the disease is of tuberculous origin. (Figure 9.)

MANAGEMENT

Undoubtedly, many cases of uncomplicated regional enteritis subside spontaneously or respond to conservative therapy. It is my opinion that many such cases occur but are not diagnosed. If such cases are recognized and do not develop surgical complications, conservative therapy may be justifiable. However, when complications do develop, surgical therapy should be promptly administered. As the etiology of the disease is undetermined, no specific nonsurgical remedy is known. General supportive care accompanied by a nonirritating diet is important. Our experience with the use of various antibiotics including the sulfa drugs, penicillin, and streptomycin has not been encouraging and has shown no improvement over conservative therapy without the use of these drugs.

IN THE acute stages of this disease the diagnosis often is established by abdominal exploration, usually because of the mistaken diagnosis

of acute appendicitis. If this occurs and the appendix is found to be uninvolved it should not be removed because of the danger of fistula formation. If an exploratory operation reveals an uncomplicated acute regional enteritis and the patient has not been prepared for intestinal surgery, radical surgical procedures should be delayed until the disease has become more chronic and the patient has been adequately prepared. In the past, resection of the entire diseased portion of the affected bowel and mesentery has been advocated. This carries a fairly high mortality rate and is followed by frequent recurrence of the disease in spite of the radical nature of the procedure. Ileotransverse colostomy has been utilized, anastomosing the ileum proximal to its highest diseased portion to the transverse colon. When the ileum distal to this anastomosis has not been divided, good results have been infrequent. This operation often is followed by an extension of the disease in the small bowel and to the colon in the region of the anastomosis.

Ileotransverse colostomy with exclusion of the ileum distal to the anastomosis has proved to be a very satisfactory procedure. Garlock has reported a series of nearly 100 patients on whom this operation was performed with no mortality

and with a high incidence of remission of the disease. He reported spontaneous healing of fistulas in almost all cases where this complication existed by this more conservative operation of ileotransverse colostomy and exclusion of the ileum. Such results support preference of this procedure over radical surgical treatment of abdominal fistulas and extensive resection of diseased bowel segments.

CASE REPORT

The patient who has kindly consented to appear before you today is a doctor of dental surgery. As is so common among professional people, he not only has developed an uncommon disease but also has developed numerous complications and an unusually extensive bowel involvement. Dr. G., who is 37 years of age, informs me that when he was a young lad he was kicked in the abdomen by a horse. He was confined to bed for a few days. Following this accident he developed abdominal pain and discomfort whenever he attempted strenuous athletic training. The history of this injury is of interest because of the frequent mention of abdominal trauma as an etiologic factor in cases of regional enteritis.

In 1931, at the age of 20, Dr. G. first noted mild indigestion accompanied by belching and abdominal tenderness. His symptoms were not severe at this time. Medical investigation failed to reveal the nature of his illness. One year later severe abdominal pain occurred the day following an unusually heavy evening meal. The pain was intense and diffuse and spread throughout the entire abdomen. He was considered a surgical emergency with a diagnosis of peritonitis and was immediately operated. At this operation the ileum was found to be spongy, inflamed, and dilated and evidently had ruptured producing a diffuse peritonitis. The abdomen was drained but no bowel was removed or repaired. His postoperative convalescence was complicated by abdominal drainage, hiccoughs, and vomiting. At the end of six weeks his drainage had ceased and he was sufficiently improved to be discharged from the hospital. He was symp-

tom-free for a period of four years, during which he had no pain and had gained in weight to a maximum of 175 pounds. He then developed cramping pains immediately after meals. His description of the pain is quite typical of that seen in the early obstructive stages of regional enteritis. Weakness and weight loss were progressive. Diarrhea, which usually is seen in this disease, was not noted.

IN 1935 a diagnosis of regional enteritis was established and he again was operated. In a two-stage procedure an ileotransverse colostomy was performed with removal of a portion of the terminal ileum and right colon. An abdominal fistula followed this operation. Four subsequent operations were performed in an effort to close the fistula but all were unsuccessful. In 1936, after the removal of more small intestine, the fistula healed.

The patient was symptom-free from 1936 to 1942 when he had a recurrence of typical symptoms of regional enteritis. He was reoperated and because of extensive involvement of the small bowel, his entire ileum and all but approximately 3 feet of jejunum were removed. Therefore, this patient is now living with only 3 feet of small intestine and with only the left half of his colon still present. In spite of the small amount of bowel remaining, this patient whose weight fell to 96 pounds in 1942, has gradually gained to his present weight of 140 pounds. When he was questioned today the following information was obtained: He is able to eat all types of food except raw vegetables, particularly onions and radishes which produce heartburn and indigestion. He has four meals a day and develops hunger if he does not eat every three to four hours. Although he indulges in little physical activity, his appetite is excessive and he states that he eats far more food than the average hard working man.

The patient has an average of four to five stools each day and if the daily bowel movements are less, he has a feeling of constipation. The stools are soft and fetid, with considerable fermentation.

It is apparent that this patient, due to the small amount of remaining intestine, does not thoroughly utilize the food which he eats but by the ingestion of large amounts of concentrated food he is not only able to maintain an adequate state of nutrition but has gained 45 pounds. However, two years ago he developed what was diagnosed as pernicious anemia which is being treated by the injection of liver extract.

This patient has had a total of eleven opera-

tions for regional enteritis and its complications. Since his last operation in 1942 he has had no pain or other symptoms suggestive of a recurrence of the disease. He is able to carry on his practice and states he can lead a fairly normal life with few restrictions. He has asked the question "Might I get this disease again?" That question cannot be answered with certainty but after five years of freedom from symptoms, prospect of a permanent cure is encouraging.

REFERENCES

1. CROHN, B., GINSBURG, L., and OPPENHEIMER, G. D.: Regional ileitis, pathologic and clinical entity. J.A.M.A. 99:1323-1329, 1932.
2. GARLOCK, JOHN H.: The present status of the problem of regional ileitis. Am. J. Surg. 72:875-878 (December) 1946.
3. SHAPIRO, R.: Progress of medical science surgery. Regional ileitis; a summary of the literature. Am. J. M. Sc. 198:269-292 (August) 1939.
4. STIERLIN, E.: Roentgenography in the diagnosis of ileocecal tuberculosis and other diseases of the intestine. Munchen. med. Wchnschr. 58:1231-1235, 1911.

New Books Received

GLOMERULAR NEPHRITIS: DIAGNOSIS AND TREATMENT. By Thomas Addis, M.D., F.R.C.P. (Edin.). 338 pages. 1948, The Macmillan Company, New York. Price \$8.00.

IDENTIFICATION OF TUMORS. By Nathan Chandler Foot, M.D., Professor of Surgical Pathology, Cornell University Medical College; Surgical Pathologist to New York Hospital. 397 pages, 241 illustrations. 1948, J. B. Lippincott Company, Philadelphia. Price \$6.00.

MALE HORMONE THERAPY. A Refresher Course. 310 pages. 1948, Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

THE HOSPITAL CARE OF NEUROSURGICAL PATIENTS. By Wallace B. Hamby, M.D., F.A.C.S., Professor of Neurology and Neurological Surgery, University of Buffalo School of Medicine. 156 pages. 2nd Edition. 1948, Charles C Thomas, Springfield, Illinois. Price \$3.00.

TEACHING PSYCHOTHERAPEUTIC MEDICINE. An experimental course for general physicians given by Doctors Walter Bauer, Douglas B. Bond, Henry W. Brosin, Donald W. Hastings, M. Ralph Kaufman, John M. Murray, Thomas A. C. Rennie, John Romano, and Harold G. Wolff. Edited by Helen Leland Witmer, Ph.D. 464 pages. 1947, The Commonwealth Fund, New York. Price \$3.75.

Diagnosis and Treatment of Myasthenia Gravis

HENRY R. VIETS*

HARVARD UNIVERSITY MEDICAL SCHOOL, BOSTON

MYASTHENIA gravis is a somewhat rare disease—not quite so rare as we thought it was ten years ago, but still a disease of which there are probably not more than 1500 cases in this country. It is a simple disease in one sense of the word, for it is characterized by a weakness of muscular action entirely due to excessive or pathologic fatigue. That is the only symptom of myasthenia gravis. It might be said that it is an exaggeration of normal fatigue of voluntary muscles, because in each case where the muscle is fatigued it will return to normal, or nearly normal, on rest, exactly as muscles return to normal after they are fatigued in normal persons. It is important, I think, to grasp the fundamental concept of this disease because it simplifies the whole problem in that you have only one possible symptom, namely, fatigue of some voluntary muscles.

The interest in the disease lies partly in the fact that certain groups of muscles are likely to be involved at the beginning and there may be a shifting from one group to another. The

disease, moreover, progresses by spontaneous remissions and relapses. It covers a long period of time. Up to about 1935 the mortality was between 50 and 75 per cent, so its name, "grave myasthenia," was indeed justified. I have estimated that in one hospital where I am working, over a period of thirty years prior to 1935 we had only 30 cases, one a year, and that half of those cases died in the hospital and another half died within a year after leaving the hospital. This was indeed a fatal disease.

The mortality from the disease at the present time, however, is probably less than 10 per cent, so that we have reduced the death rate from roughly 50 to 75 per cent down to less than 10 per cent.

Myasthenia gravis has been well known for many years. As a matter of fact, it was described even in the seventeenth century. The two names that stand out in the nineteenth century are Erb and Goldflam.

The original paper of Erb was published in 1879, while Goldflam's first report appeared in the year 1893.

By 1900 the disease was well recognized clinically.

When we consider the number of cases that we have seen since 1935—since which time we have had a method of diagnosis and a means of alleviation of symptoms—the incidence has in-

From the Myasthenia Gravis Clinic, Massachusetts General Hospital.

*Lecturer on Neurology, Harvard University Medical School, Boston.

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HENRY R. VIETS

creased greatly. At the Massachusetts General Hospital, for instance, from 1905 to 1935 we had this scattering of cases that I have already mentioned. Since 1935 we have seen more than 200 cases. That means a number of things. Our interest in the disease has increased; more cases are being discovered because we have an adequate diagnostic test; and the number of cases that survive over a long time has increased because they do well under treatment.

I doubt whether there are any more cases in the United States today than there were ten or fifteen years ago, but a lot more have been discovered than formerly. That is the very point of this paper, because I want to show you how such cases can be discovered and how these patients can be treated.

The presenting symptoms of the disease vary a good deal. There is always a fatigue of voluntary muscles, but early in the course of this disease certain muscles are more easily fatigued than others. When we analyze the histories of our patients, we see that the muscles that have

to do with movement of the eyes and eyelids are most frequently affected. In a little over 45 per cent of the cases the first symptoms often are ptosis and diplopia. Most of these patients, therefore, go to the ophthalmologist, though they may be seen first by the general practitioner. If you have this disease in mind—which unfortunately many physicians do not—you will consider seriously the possibility of myasthenia gravis when you have a patient with a sudden ptosis and double vision without obvious cause, the symptoms fluctuating during the day or during the week or month, and usually being better in the morning after a night's rest and worse in the afternoon.

THE SECOND group is even more important because they have no distinctive and outstanding muscle signs such as ptosis and diplopia which you see as soon as the patient comes into your office, but they come in on account of general weakness, fatigue in walking upstairs, difficulty in raising their arms and doing ordinary household tasks. This is the large group, about 30 per cent of the total, that have general muscular weakness and is confused most often with cases of neurasthenia. It is probably the group that is less often diagnosed than the cases with special symptomatology such as ptosis and diplopia.

Another group, comprising about a fifth of the cases, have dysphagia and dysarthria. Here again there is a fluctuation in the symptom—the patient may have no trouble in swallowing breakfast but will have difficulty with luncheon and increasing trouble with supper. Speech is affected the same way: after a few minutes the voice becomes nasal, and always on rest there is a tendency to restoration of function to normal. That is the key of the whole disease.

There is still another group in which neck weakness is an important feature and is sometimes the only symptom. A patient will notice suddenly one morning on washing his face in the bowl that he will start to lift up his head and he will be unable to do so. If he rests a

few minutes he can lift his head normally.

Thus the ophthalmologist may see the ptosis and diplopia cases; the laryngologist may see the dysphagias and dysarthrias; the general weakness group usually falls to the general practitioner, as does the group affected only with neck weakness; but any of them may be seen by anyone at any time.

Let us look at the age group, which is another important point. You will find in the textbooks that for many years everyone thought this was a disease of young people, of adolescence or the third decade of life. It is in part, but when we come to analyze our cases they spread all the way from the very earliest years of life to well into the eighties, and interestingly enough there is a large group of patients between 60 and 70 which we had never discovered before. These are the cases that in the past were almost inevitably missed in diagnosis because they were confused with the patients who at that age have obstructions of the larynx due to cancer, bulbar palsy with speech defects, vascular changes in the brain stem, and other diseases of a degenerative type. The superintendent of a hospital began to have his first symptom when he was over 70, and I must say the diagnosis was missed for five or six months because ten years ago we were not thinking in terms of this disease. One should look at the older age group as a very important and formerly undiagnosed group of patients with this disease.

When we put those groups into decades, it is clear that the disease may appear in any decade during the patient's life except perhaps over 80 and rarely under 10. A few cases occur in infants. I have not personally seen any, but there are some in the literature. It is possible that those are cases of myasthenia gravis, but it is not easy to be sure. The patients most frequently seen are young adults or people in middle life.

Between 1930 and 1935 we had developments in our knowledge of this disease which revolutionized our whole attitude toward it. In 1931 Aeschlimann and Reinert were investigating physostigmine and were making up

synthetic analogues. One they called prostigmine now known as neostigmine. This drug proved to be invaluable for it turned out to be a diagnostic as well as a therapeutic agent for the disease. It is the only drug that has any marked effect upon myasthenia gravis. There are others that have some effect, but this is *the* drug that has the most marked effect and the one that is used as a diagnostic test.

As a diagnostic test, the dosage is 1.5 mg. of neostigmine methylsulfate given subcutaneously. The methylsulfate is the soluble form put up in an ampule, and to that is added some atropine to overcome the intestinal stimulation which often goes along with the initial use of the drug. There is a diagnostic ampule now available containing the proper dose for an adult and the proper amount of atropine in one ampule. If there is reasonable doubt in your mind regarding the diagnosis in the early stages, one should attempt either to confirm or to discard the diagnosis with a diagnostic test using neostigmine.

There may not be reasonable doubt about the diagnosis if you are familiar with the disease, because the symptomatology is so definite, so unique, and so characteristic that a patient having a muscular weakness that recovers to normal after a period of rest and then relapses on effort is not found in any other disease. With a good history and a knowledge of the background of this disease in mind, the diagnosis is usually exceedingly easy from the clinical record alone. On the other hand, if you are not thinking about the diagnosis, and if you consider the disease to be a rare one, you need some sort of reinforcement of a presumptive diagnosis of myasthenia gravis.

Neostigmine is found to be an almost specific remedy in the diagnosis and treatment of this disease. It overcomes in large part the one principal symptom, namely, muscular weakness, and because of that we use it as a diagnostic agent. If a patient has ptosis, diplopia, facial weakness, difficulty in chewing, difficulty in talking, or difficulty in swallowing, and the



Figure 1. Prostigmine diagnostic test. Alleviation of symptoms after injection of 1.5 mg. of prostigmine methylsulfate plus 0.6 mg. of atropine sulfate ("the diagnostic ampule"). The patient, aged 32, had had symptoms for over two years. Since 1940, when the diagnosis was first made, the patient has been fully adjusted on 4 to 6 tablets of prostigmine bromide, 15 mg. each, taken by mouth.

drug is injected subcutaneously in the appropriate amount as given in the diagnostic ampule, the patient will, in about 20 to 30 minutes, recover entirely, or in very large part, all use of the affected muscle. It is perhaps one of the most dramatic changes that we see in all medicine.

Figure 1 illustrates this response to the drug. This patient had dysarthria and dysphagia, ptosis and diplopia. I think you can see the bilateral facial weakness. That is a typical picture of myasthenia gravis with the facial and cranial muscles involved. Fifteen minutes after the injection of neostigmine the whole picture is changed—the ptosis disappears; the diplopia is gone; the facial muscles are now in action; chewing, swallowing, and talking are normal, and the diagnosis is unmistakable. No other disease responds in this remarkable way. Other diseases may give a slight response, but certainly under 10 per cent, whereas the response in myasthenia gravis runs up to 85, 90, or even 100 per cent as in this picture. Therefore the diagnosis is clinched if this response is present.

This test was first reported in 1935 by Dr. Schwab and myself, and I think that in the twelve years that have elapsed it is fair to say

it has been accepted as a diagnostic test. As we have used it in more than 200 patients I think that we were never in doubt in regard to the diagnosis of myasthenia gravis if the response was in the 85 to 90 per cent group; if it was down below 25 per cent, there was a reasonable doubt about the diagnosis, and most of those cases do not turn out to be myasthenia gravis. It is, therefore, a sound test. If you use it and the response is good, the diagnosis cannot be anything but myasthenia gravis.

We also have another method of diagnosis in certain cases which is very satisfactory. If the patient has dysphagia as one of the symptoms, you can study that difficulty in swallowing under the fluoroscope with an ordinary barium meal, and then after injection of neostigmine, you will find in 20 to 30 minutes that the swallowing reflex is absolutely normal. Here again it is a dramatic test for the disease and it is unmistakable; no other disease could possibly do this. In this way you differentiate myasthenia gravis from all the other diseases causing difficulty in swallowing. Should your patient have dysphagia as one of the symptoms or as the principal symptom, this study under the x-ray before and after neostigmine will make the diagnosis quite certain.

As for the treatment of the disease, the first drug that was used to any extent was ephedrine. Dr. Harriet Edgeworth, in this country, showed as early as 1930 that this was of some value, and it is still of some use. It falls into the group of about 10 to 15 per cent of usefulness compared with neostigmine which is 85 to 90 per cent in its usefulness.

Then Dr. Mary Walker, a London physician, first used physostigmine in 1934. Physostigmine was soon replaced by neostigmine, which is an easier drug for the patient to tolerate and has practically no side reactions of the type associated with physostigmine.

Neostigmine is used in two ways. In the diagnostic test it is always used subcutaneously. In the treatment of patients it may be used either subcutaneously or orally. All our patients

take the medicine orally in the form of prostigmine bromide, the only tablet made for oral medication. There are 15 mg. of neostigmine bromide in each tablet.

Under certain conditions we may supplement the oral dosage with subcutaneous injection, but that is rarely done, and not more than 2 or 3 per cent of my patients take the drug subcutaneously. They are all adjusted to oral neostigmine bromide.

Theoretically this is the only possible way to treat a patient with a chronic disease that requires the administration of a drug for a period of months, years, or even possibly the rest of his life, because neostigmine treatment turns out to be a form of substitution therapy. Something has dropped out of the body, there is a chemical dysfunction at the junction of the nerve and the muscle; neostigmine is added to this myoneural junction or synapse and the chemical reaction is restored to normal, or partially so. One must think of this as a form of substitution therapy exactly as one thinks of insulin in diabetes or liver therapy in pernicious anemia.

That point is a very important one, because the minute you grasp it your whole attitude toward this disease is changed. The treatment of this disease becomes a life problem. Success can be reached only if the patient is continually under the doctor's care or observation, presumably for the rest of his life. To be sure, he may have long periods of remission in which he takes no medicine and has no symptoms. Some of these remissions have lasted for an extraordinary length of time, even as long as twenty years. Most of the remissions, spontaneous in type, last perhaps six months or a year; some of our recent remissions have lasted five years. But in spite of that one must consider the patient as one to be continually under therapy.

A BRIEF discussion of the thymus in relation to this disease is of importance. It was noted at post mortem, before the days of modern

REMISSIONS IN TWO CASES OF MYASTHENIA GRAVIS IN WHICH PROSTIGMINE WAS REQUIRED TO CONTROL SYMPTOMS

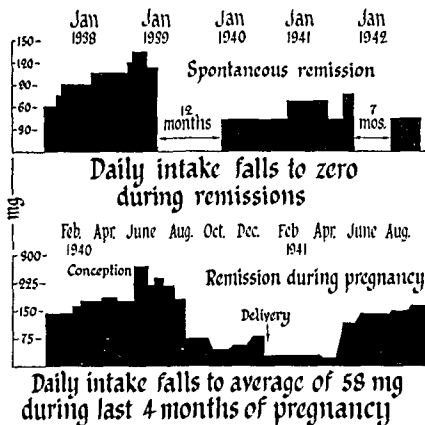


Figure 2.

treatment, that the thymus was changed in a person who had myasthenia gravis. In about 50 per cent of the cases hyperplasia was found, in some cases tumor formation, or thymoma. That led to an investigation of the relationship, if any, between the thymus gland, so-called, and myasthenia gravis. It is obviously a difficult problem. We are dealing with a structure that we know little about; we do not actually know whether it is a gland (particularly in the adult), whether it has any hormonal secretion, or what possible relationship it could have to this disease. Those matters are still uncertain. The observations on the thymus at post mortem led, however, to the surgical removal of the thymus gland or thymoma in a certain number of patients in recent years. One series in England has reached 100, and in this country some physicians have removed at least 50, others 20. I suppose there are 250 patients that have had thymectomy.



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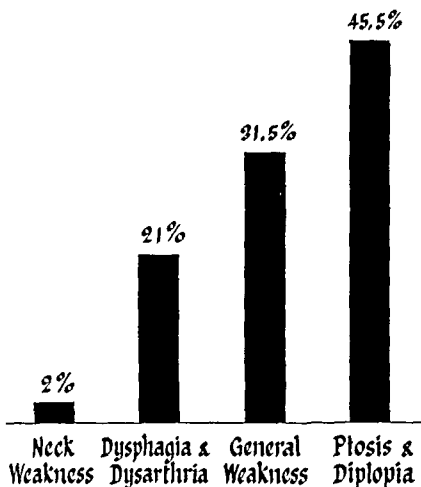
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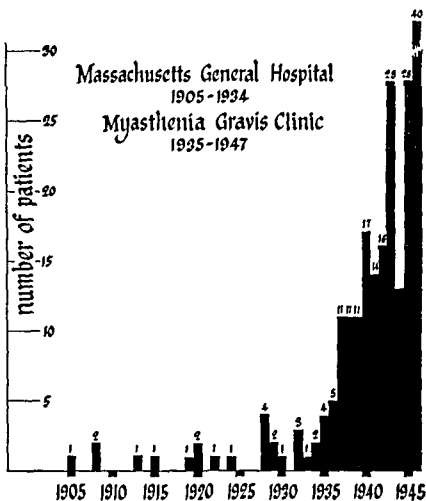
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PRESENTING SYMPTOMS IN 200 PATIENTS WITH MYASTHENIA GRAVIS



CASE INCIDENCE OF MYASTHENIA GRAVIS



fined to bed. A few months ago her doctor began to think of myasthenia gravis as a possible diagnosis. An injection of neostigmine was given and in 15 or 20 minutes the patient got up out of bed, walked around, raised her arms, and was almost normal. It is extremely interesting that for ten years a patient should be allowed to go undiagnosed with a disease that has such remarkable possibilities from therapy. She has begun to be adjusted on oral neostigmine. At the present time she is taking 6 tablets a day, one at 5:00, one at 7:00, one at 10:00, one at 12:00 noon, one at 5:00 and one at 10:00. This she has done for three months, and during that time she has been able to be up every day, drive

20 miles in her automobile, and be in reasonably good condition.

I have an idea that she is not quite fully adjusted on treatment as yet. The average intake in my clinic is not 6 or 7 pills a day, but nearer 10 or 12 a day. If that amount is given and if the lateralization of the dose is correct throughout the day, a patient ought to be practically free from symptoms at all times. One does not reach that height always, but that is the aim—to balance the neostigmine against the symptoms of the disease and to make the patient as well as possible. I have five or six doctors with myasthenia gravis, and I am glad to say they have all continued in practice, although under a somewhat modified schedule.

WHAT ARE the results of thymectomy? They are difficult to evaluate. Here you are dealing with a disease that has spontaneous remissions and relapses. A patient may do very well and even have a "cure" in the sense that he has no symptoms and needs no neostigmine after thymectomy. On the other hand, for each patient who has had a thymectomy I can show three patients from my clinic who have not had a thymectomy who do exactly as well. So you see that is a difficult problem to resolve. I am still not in a position to tell you whether thymectomy is of value in this disease or not, and I think that is the general consensus in this country. It is not necessarily the way people feel throughout the world. But I should like to say that we are still in the experimental stage as far as thymectomy is concerned. I rarely advise it. I advise it only in patients who

AGE AT ONSET OF SYMPTOMS OF 200 PATIENTS
WITH MYASTHENIA GRAVIS

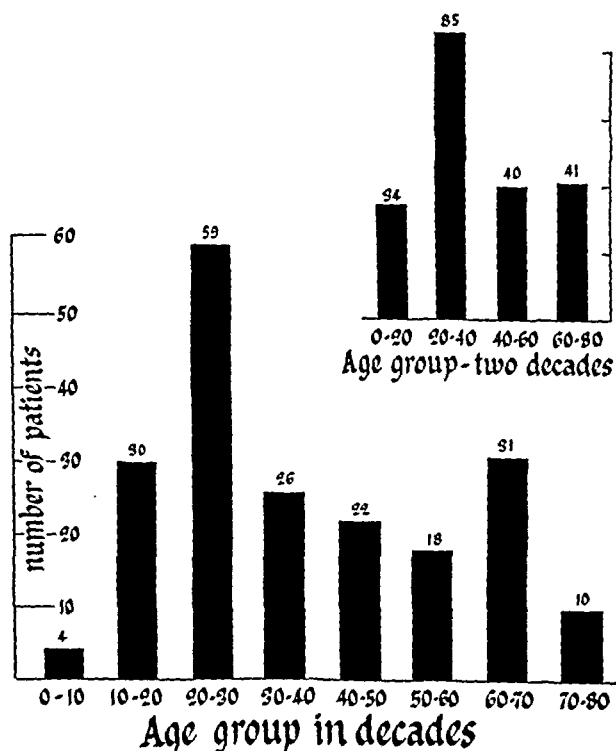


TABLE 1
STATISTICAL SUMMARY
MYASTHENIA GRAVIS CLINIC (1935-1946)

	NUMBER	PER CENT
Cases diagnosed since 1935.....	200	
Deaths since 1935.....		20
Patients living, December 31, 1946.....	159	
Excellent adjustment on treatment.....		52
Good adjustment on treatment.....		39
Poor adjustment on treatment.....		9
Partial remissions.....		17
Complete remissions.....		14

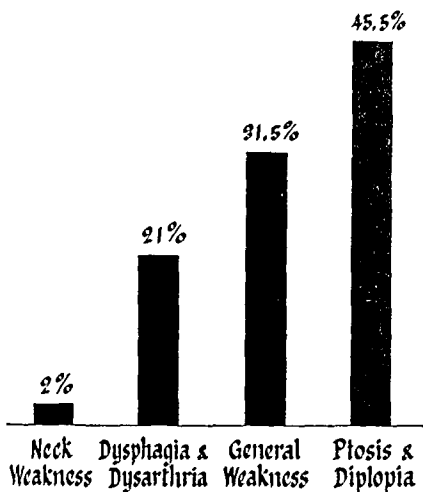
have not done well under their medical treatment, and that, I think, is justified.

Figure 2 shows the spontaneous remissions that occur. The chart is based on the amount of neostigmine that the patient takes. There is a twelve-month period in the top chart showing the record of a patient without any symptoms and with no need for medicine. Then a relapse occurs, and there follows a seven-month remission. Remission often happens during the last two trimesters of pregnancy. The remission may last for a number of months after pregnancy is terminated.

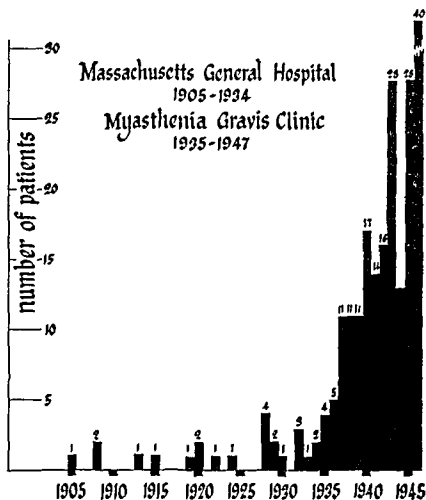
A general summary of the clinic cases shown in Table 1 gives you an idea of how things are going at the present time: 200 patients with a 20 per cent death rate since 1935. I told you the mortality was probably under 10 per cent. You must realize that in this age group, which goes up to 80 years, there is a natural mortality on account of age, so I think one ought to reduce the mortality under modern treatment to 10 per cent. Half of the patients are well adjusted on treatment; another group has good adjustment; some, about 10 per cent, have poor adjustment, which is the best we can do. Partial remission occurs in 17 per cent; complete remission in about 15 per cent.

The following case of a woman patient shows an interesting history. For ten years, since she was 32 years of age, she was almost bedridden, at least houseridden. She could get up and do a little work, she could raise her arms slightly, but for most of the time she was con-

PRESENTING SYMPTOMS IN 200 PATIENTS WITH MYASTHENIA GRAVIS



CASE INCIDENCE OF MYASTHENIA GRAVIS



fined to bed. A few months ago her doctor began to think of myasthenia gravis as a possible diagnosis. An injection of neostigmine was given and in 15 or 20 minutes the patient got up out of bed, walked around, raised her arms, and was almost normal. It is extremely interesting that for ten years a patient should be allowed to go undiagnosed with a disease that has such remarkable possibilities from therapy. She has begun to be adjusted on oral neostigmine. At the present time she is taking 6 tablets a day, one at 5:00, one at 7:00, one at 10:00, one at 12:00 noon, one at 5:00 and one at 10:00. This she has done for three months, and during that time she has been able to be up every day, drive

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Diagnosis and Treatment of Bronchial Asthma

LEON UNGER, M.D., HERMAN A. LEVY, M.D., ALBERT H. UNGER, M.D.,
AND ISABELLE B. EISELE, M.D.

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL AND WESLEY MEMORIAL HOSPITAL, CHICAGO

DIAGNOSIS

Bronchial asthma is an allergic condition characterized by wheezing, dyspnea, orthopnea, cough, associated with rhinitis and partial obstruction of lower air passages. Most cases: (a) history previous attacks, allergy in family or other allergies in patient; (b) generalized wheezing and prolonged expiration; (c) eosinophilia in blood and especially in sputum; (d) relief from epinephrine and/or aminophylline; (e) positive skin tests. Any one finding can occur in nonallergic conditions.

Complications

Chronic asthma leads to emphysema and deformed chests. Bronchitis, sinusitis, pneumonitis, atelectasis, and spontaneous pneumothorax may occur.

Differential Diagnosis

From all other causes of dyspnea, wheezing and cough, e.g., acute cardiac dyspnea, fibroid tuberculosis, silicosis, substernal goiter, lung carcinoma, foreign bodies. Inspiratory wheezing indicates obstructive condition; rare in bronchial asthma.

Causes of Attacks

Often easily discovered, but in some cases every diagnostic method is used; (a) careful history; (b) relief or return of symptoms by avoidance or exposure to cause, e.g., dog hair, egg; (c) relationship of symptoms to atmospheric pollen or mold counts; (d) skin tests, scratch and intradermal, clinically corroborated.

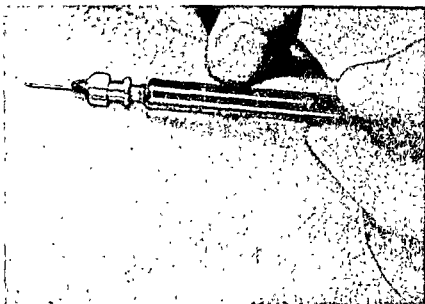
TREATMENT

Preventive: (a) Children of allergic parents: avoid pets, orris root, feathers, excess house dust and pollen. Add new foods singly. Prompt allergy survey if "eczema," "bronchitis," rhinitis, hay fever, or wheezing are present. (b) Allergic persons: avoid dusty occupations: farmer, baker, furrier, miller, domestic.

A national campaign for education in
and prevention of asthma is a must.

Specific: (a) *Avoidance* of allergens, e.g., dog, orris root, house dust. May be sufficient. (b) *Hyposensitization:* injections of increasing amounts of extracts of important allergens which cannot be avoided, e.g., house and occupational dusts, pollens, molds, orris root. Results usually good.

Symptomatic: (a) Reassuring patient most important single measure. (b) Epinephrine: subcutaneous 1:1,000; intramuscular 1:500 in oil; by inhalation 1:100 spray. (c) Aminophylline: $3\frac{3}{4}$ to $7\frac{1}{2}$ gr. intravenously; 10 gr. in water, or $7\frac{1}{2}$ gr. suppository rectally. (d) Ephedrine: $\frac{3}{8}$ to $\frac{1}{2}$ gr. orally. (e) Glucose: liter 5 per cent intravenously with aminophylline. (f) Air-filtered, dust-free room (hospital or home). (g) Iodides, apomorphine, syrup ipecac, mild sedation. (h) Do not use morphine—too dangerous. (i) Penicillin or sulfonamides for infectious complications; little effect on asthma itself. (j) Vaccines, x-ray therapy, removal foci infection, bronchoscopy, psychotherapy, estrogens.



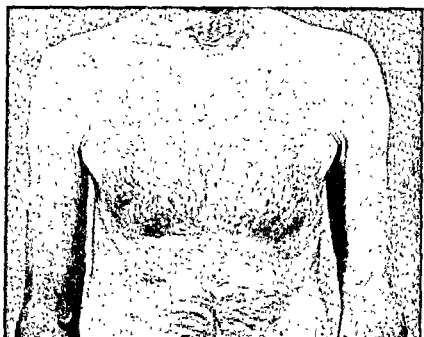
Technic of intracutaneous test (tuberculin syringe, 27 gauge needle).



Technic of scratch test (forearm, cataract knife).



Chronic bronchial asthma with severe emphysema. Note increased antero-posterior diameter.



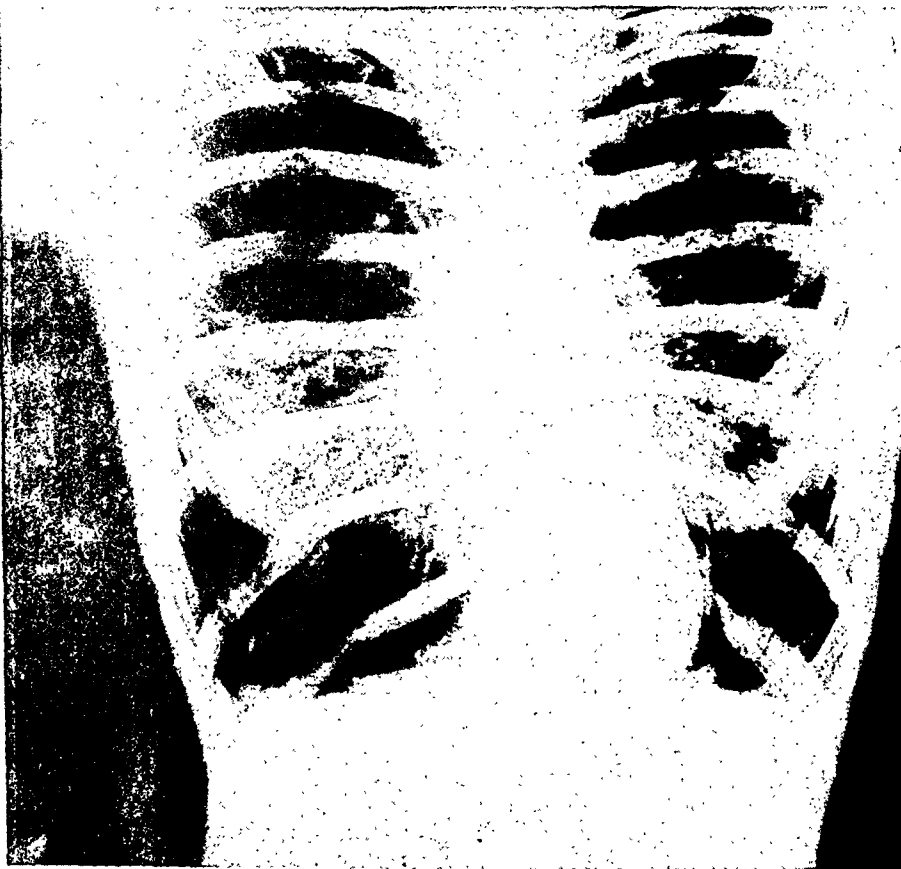
Bronchial asthma with emphysema.



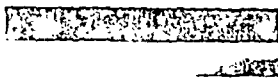
Bronchial asthma (chronic) with emphysema. Note increased antero-posterior diameter.



Large nasal polyps in an asthmatic patient. Removal of polyps frequently relieves asthmatic symptoms.



Severe chronic asthma with marked emphysema: ribs almost horizontal, wide intercostal spaces, small heart, depressed diaphragm (practically no movement on fluoroscopy). Also note three small areas spontaneous pneumothorax due to rupture emphysematous blebs. Emaciated woman, 28, asthma since infancy, weight 70 lbs. on admission to hospital. Marked improvement with gain to 104 when given high caloric diet and injections of adrenal cortex plus extra salt. Positive skin tests for molds, pollens, house dust. Good response to continuous aminophylline intravenous therapy.



R. P. Man, 32, chronic asthma, hay fever, bronchiectasis (note cavities in lower left lobe, with slight involvement right lower lobe). Lobectomy (left lower lobe) at Wesley Memorial Hospital, May 1946, because of persistent malnutrition, cough, showers of moist râles and frequent bouts of pneumonitis with fever, chills, hemoptysis. Excellent results. Left hospital in two weeks and has gained about 20 pounds. Lungs now almost clear. Continues injections of pollen, mold, and house dust extracts.





ANCIENT AND MEDIEVAL PERIOD (TO 1500 A.D.) (PERIOD OF CONFUSION AND MANY REMEDIES) Moses Maimonides, Jewish philosopher and physician, treating Sultan Almalik for asthma. Treatment: enemas, poultices, laxatives, cupping, fomentations and venesection. All causes of difficult breathing confused with bronchial asthma.

HIPPOCRATES (460-357 B.C.) "Father of Medicine" recognized "spasmodic asthma." Believed cold and moisture the principal causes, especially in children.

CELSUS (25 B.C.-7 A.D.) Divided difficult breathing into "dyspnea" (mild and chronic) & "orthopnea" (acute and more severe). "Orthopnea" (acute and most severe)

ARETAIUS OF CAPPADOCIA (2nd cent. A.D.) First accurate description of asthma, separated asthma from orthopnea. "If heart be affected patient cannot long survive."

GALEN (130-200 A.D.) "Prince of Physicians" Four humors: the blood, phlegm, black and yellow bile. His ideas influenced writers through the 17th century.

MOSES MAIMONIDES (1135-1204) Jewish philosopher, Talmudist physician, wrote *Treatise Concerning Asthma*. Recognized different patients had different sensitivities.





MODERN PERIOD (SINCE 1900): CLINICAL. Aminophyllin in 5% glucose solution is being injected into vein of an asthmatic patient in a dust-free, air-filtered hospital room. Skin-testing is by scratch and intradermal methods, both essential in many cases. Positive reactions should be clinically corroborated.

CHEVALIER JACKSON (1854-)
Famous bronchoscopist, whose research has increased the knowledge regarding asthma. "All is not asthma that wheezes."

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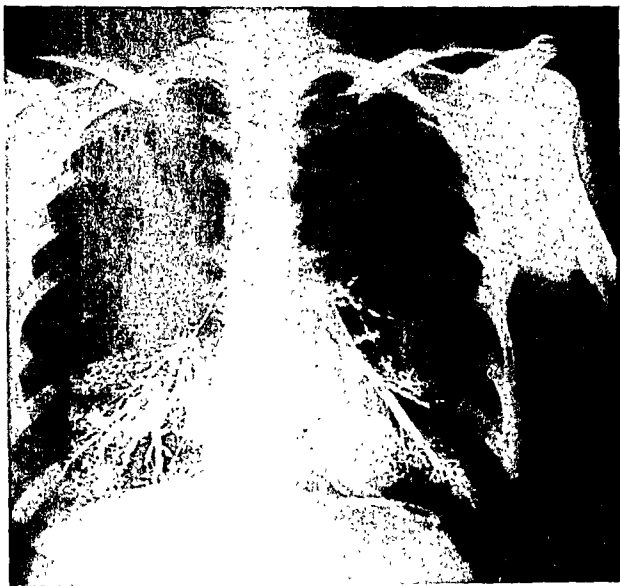
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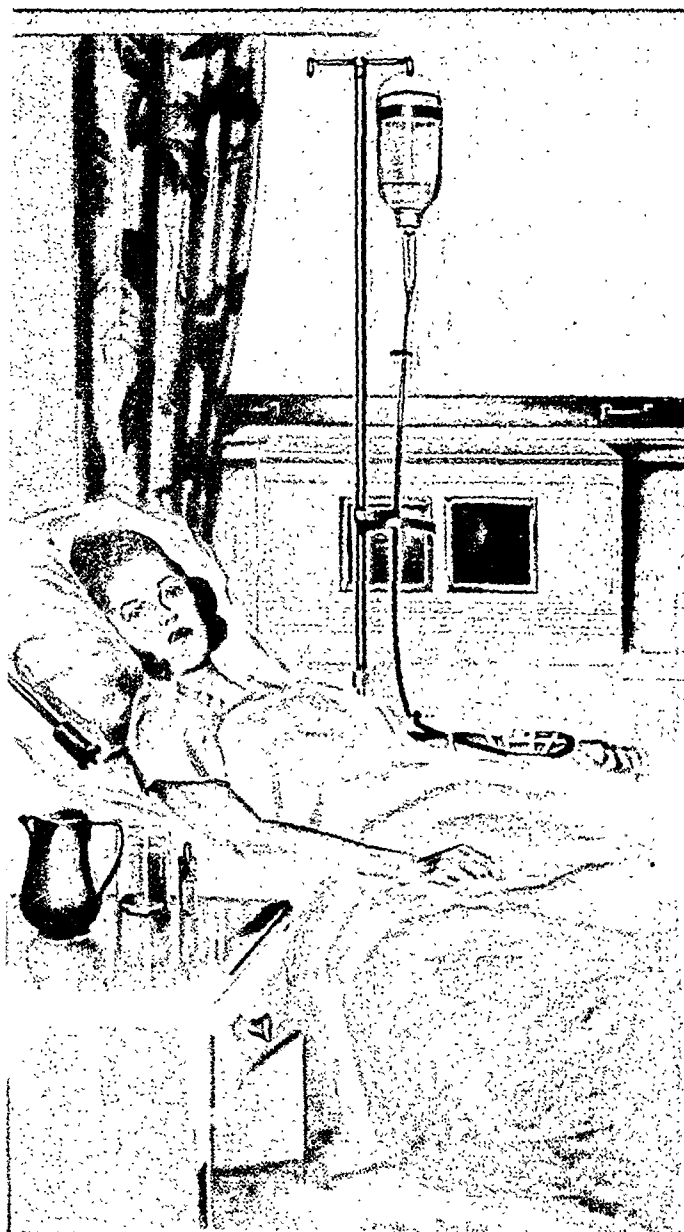
WARREN TAYLOR VAUGHAN (1893-1946) Pioneer in allergy, especially in hayfever, food allergy and asthma. Author, *Practice of Allergy*. Outstanding investigator.



40-year-old woman with chronic asthma and moderate emphysema. Skin tests practically negative and response to treatment fair only. Note anatomy of trachea, bronchi and smaller branches as shown by instillation of iodized oil. Bronchiectasis minimal. Fluoroscopy: poor expansion diaphragm.



81-year-old woman entered hospital with diagnosis of bronchial asthma, but re-examination revealed inspiratory (stridorous) wheezing rather than expiratory, and dullness and decreased breath sounds below right clavicle. No apparent goiter but x-ray showed large mass which pressed against esophagus, trachea and right main bronchus. Diagnosis: substernal thyroid (nontoxic). Removal urged but patient refused. Wheezing, dyspnea and orthopnea continued with death in about four months. Autopsy: huge substernal goiter with much colloid. Terminal bronchopneumonia. Substernal goiter not infrequent cause of wheezing and is mistaken for asthma.



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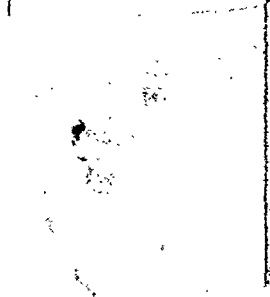
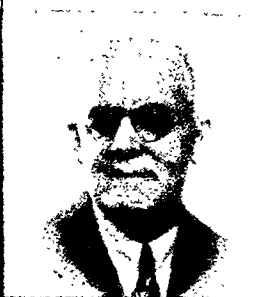
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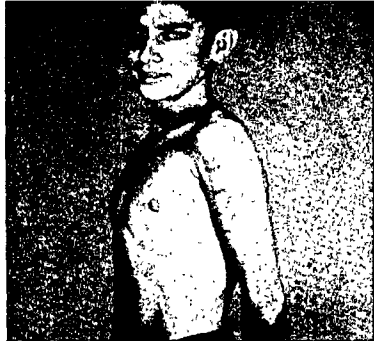
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(Above left) Typical chest of boy with bronchial asthma since infancy. Sensitive to numerous allergens.

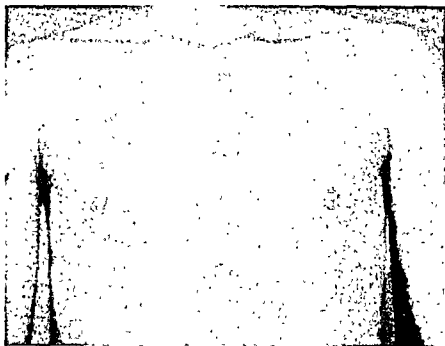
(Above right) Chest of same patient showing characteristic pigeon-breasted deformity due to chronic asthma and resultant emphysema.

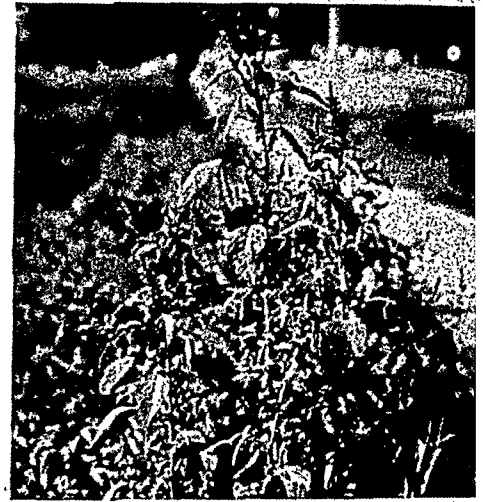
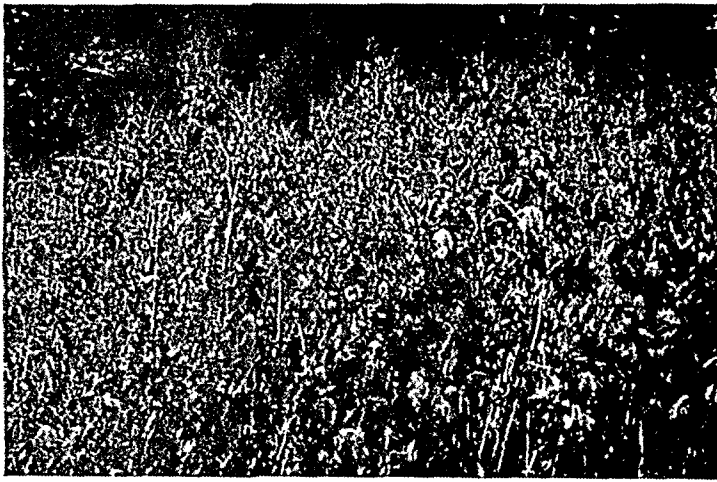
(Right) Bronchial asthma with pronounced barrel-chest characteristic of older emphysematous patients.

(Far right) Boy, 15, chronic asthma with emphysema. Responded to avoidance and hypsensitization.

(Below left) Asthmatic emphysema and barrel-chest deformity of an older boy as contrasted with pigeon-breasted enlargement of chest in younger patients.

(Below right) Same boy. Antero-posterior view.





(Above left) Giant ragweed growing to height of 6-7 feet. Pollen is carried by wind. Very important cause of hay fever and asthma in August and September.

(Above right) A patch of pigweed growing in a vacant lot. The pollen of this amaranth may be a factor in late summer hay fever.

(Left) Goldenrod. Its pollen is carried by insects and is therefore of little importance as a cause of hay fever and asthma.

(Below left) Flower of the hard maple tree. Its pollen is important as a cause of spring hay fever.

(Below center) Flowering catkin of poplar tree. Its pollen may cause spring hay fever.

(Below right) Flowers of the elm tree. The pollen is shed in large amounts in the spring and has high allergenic toxicity.



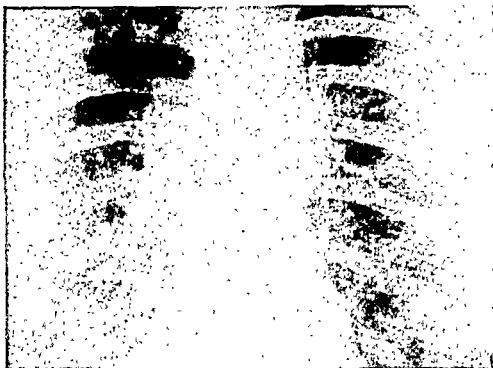
(Middle row left) Higher magnification (x315) of section of same bronchiole showing mucous plug with severe inflammation and many eosinophils.

(Middle row center) Bronchiole from same asthmatic patient. Note complete obstruction. Many eosinophils.

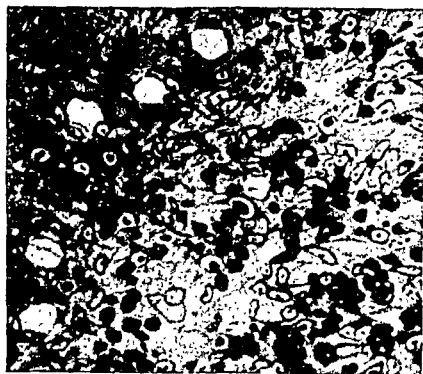
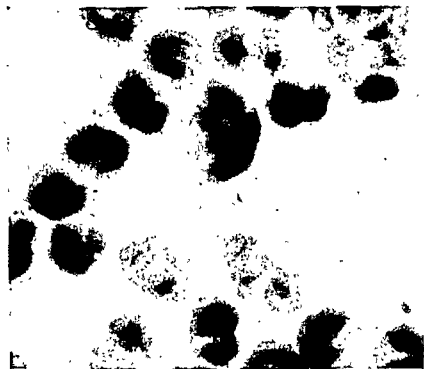
(Middle row right) Higher magnification of same baby's lung; obstruction bronchiole by mucous plug; emphysema associated.

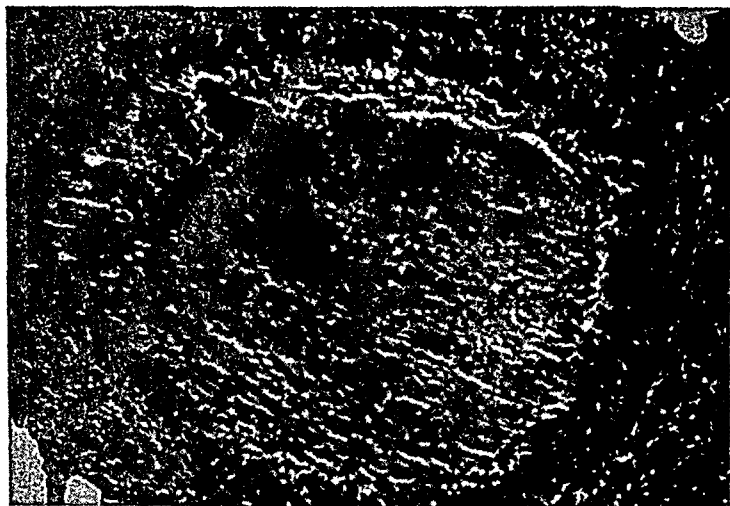
(Bottom row left) Nasal smear from patient with allergic rhinitis, showing numerous eosinophils.

(Bottom row right) Section of middle turbinate; note eosinophilia. (Courtesy, F. K. Hansel.)



(Above) Bronchial asthma, complicated by emphysema and large bleb in lower lobe. Danger of rupture of bleb with resultant spontaneous pneumothorax.





(Above) Microscopic study of lung of one-year-old patient who died 17 hours after onset attack asthma: bronchus obstructed, emphysema, eosinophilic infiltration of tissues.

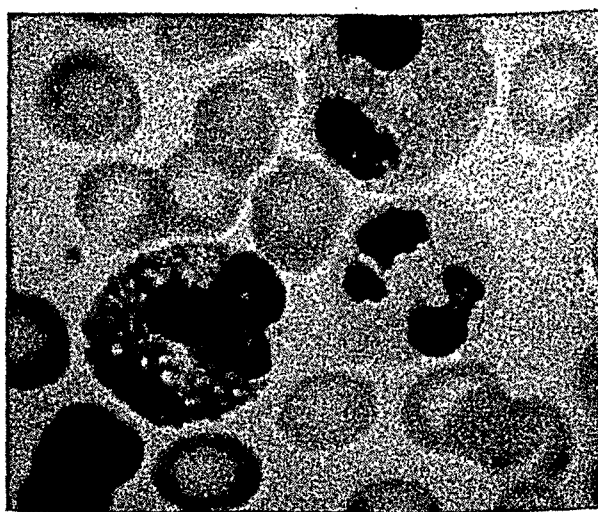
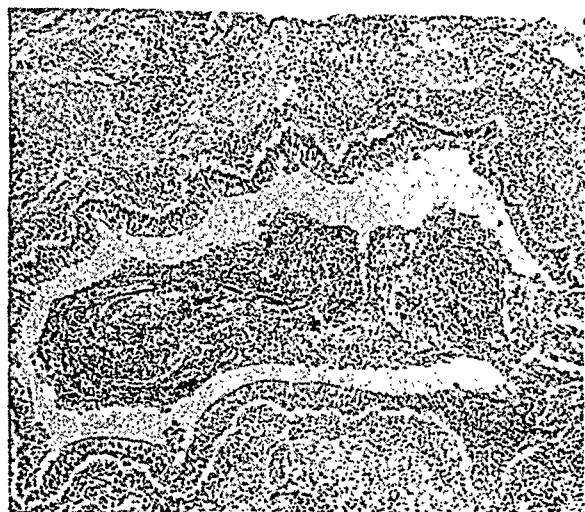
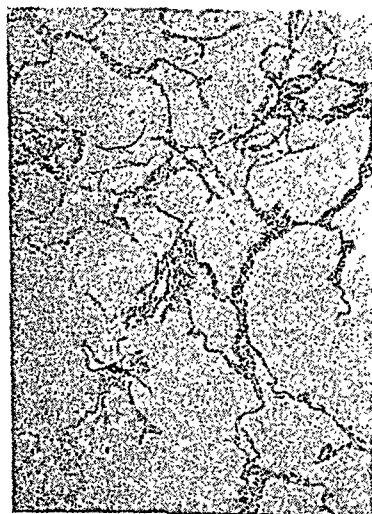
(Middle row left) Marked emphysema of lungs in an asthmatic man who died during an attack. Note the large air sacs and the tearing of partitions between them.

(Middle row center) Bronchial asthma, emphysema, mucous plugs. From lung of a one-year-old infant who died 17 hours after onset of attack of asthma.

(Middle row right) Plugged bronchus and marked emphysema; eosinophils numerous in the plug and in the walls of the bronchus. From lung of one-year-old infant who died 17 hours after onset of attack of bronchial asthma.

(Bottom row left) Bronchiole from same asthmatic patient. Note mucous plug, with incomplete obstruction.

(Bottom row right) Blood eosinophilia from asthmatic patient; note two eosinophils and one neutrophil in the smear.



CASE REPORT

First admission—J. M., a 30-year-old woman, born in this country of Italian parents, was admitted to the hospital, complaining of shortness of breath of two weeks' duration. Two years prior to admission she had begun to have severe occipital headaches of two to three days' duration at the time of her menstrual periods. The headaches had grown progressively worse. Two weeks prior to admission she had first noticed dyspnea and pounding in the chest when walking uphill or climbing stairs.

For the last fifteen years the patient had been working in the food preparation department of a chain store eight hours daily and, in addition, had been doing all the cooking and most of the washing and cleaning for a family of six in her nine-room home. A diet survey revealed that she had eaten practically no meat since childhood. At the ages of 18, 22, and 26 she had had irregular treatment with liver and iron for anemia, but she had not continued the treatments because she had felt well. She had never noticed any jaundice. Her menses had begun at the age of 16. They had been regular but scanty, and she had missed the period that was due two weeks before admission. Six weeks prior to admission she had been married and had quit her job. She had been given one injection of 2 cc. of crude liver by her referring physician two weeks before hospitalization and had been taking Lextron capsules and Feosol pills daily while awaiting admission.

Family history revealed that one sister had slight anemia all her life and another sister had had severe anemia during a pregnancy. Her mother had died at 51 of carcinoma of the stomach. Her father and three other siblings were examined. They had no anemia nor splenomegaly, and their red blood cell fragility was found to be normal.

ON PHYSICAL examination the patient was found to be extremely pale. She was not jaundiced. She weighed 122 pounds. Her blood pressure was 100 systolic, 60 diastolic. There



STEPHEN C. STAHLNECKER

was a loud, blowing, systolic murmur audible all over the precordium. The spleen was not palpable. There was no evidence of neurologic abnormalities.

Our studies showed a red blood count of 1,220,000 with 4.3 gm. (28 per cent) of hemoglobin. There was a reticulocytosis of 42 per cent. Hematocrit was 11. Our calculations revealed a mean corpuscular volume of 123 cubic micra (normal, 87 ± 5), a mean corpuscular hemoglobin of 35 micromicrograms (normal, 29 ± 2), a volume index of 1.4, and a color index of 1.1. There were 330,000 platelets per c.mm. Coagulation and bleeding times were normal.

A red cell fragility test showed hemolysis beginning at 0.45 and complete at 0.35 per cent salt solution (control, 0.45 to 0.35 per cent). The blood smear was reported as showing considerable anisocytosis, macrocytosis, and polychromasia, compatible with a diagnosis of pernicious anemia. However, a gastric analysis showed 10 units of free acid and 40 units total acidity. The x-ray examination of the chest and gastrointestinal tract revealed no abnormalities.

Congenital Hemolytic Icterus

REPORT OF CASE ASSOCIATED WITH SEVERE COLITIS CURED BY SPLENECTOMY

STEPHEN C. STAHLNECKER*

PHILADELPHIA, PENNSYLVANIA

CONGENITAL hemolytic icterus is a familial malady which was first clearly described by Minkowski¹ at the turn of the century. Its symptomatology is variable and its diagnosis is sometimes difficult, but because of the very dramatic cure effected by splenectomy, early recognition is of the utmost importance.

PATHOLOGIC PHYSIOLOGY

The etiology remains undetermined. There appear to be two possibilities: first, a defective erythropoiesis, resulting in a small, globular, hyperchromic, red blood cell, the spherocyte;²⁰ second, abnormal erythrocytes may be formed by some unknown agent acting on originally normal red cells. The patient's spleen destroys these abnormal red cells.²² His bone marrow is continually overstimulated by the demand to replace these destroyed cells. He is in a precarious state of hemolytopoietic balance, as pointed out by Doan.² If his marrow cannot maintain the pace, he becomes anemic. His excretory system may be overloaded by the excessive hemoglobin breakdown. He becomes icteric or may develop pigment stones in his biliary tract.

His spleen may become greatly enlarged. He is always subject to sudden hemolytic crisis at any time from early childhood to old age.²⁴ These crises may be fatal, they may spontaneously remit, or they may be cured and subsequently prevented by splenectomy.

DIAGNOSIS

The presenting symptoms in any particular case vary with the severity of the anemia and the degree of splenomegaly, or, as Chauffard¹⁰ noted, the patient may be more icteric than sick. Occasionally the initial picture may be that of biliary colic.

The diagnosis rests upon the discovery of a microcytic, spherocytic, hyperchromic anemia, a well-marked reticulocytosis, splenomegaly, and icterus. It is essential to demonstrate that these spherocytic cells are abnormally susceptible to hemolysis by hypotonic salt solution, as Chauffard first showed in 1907.¹⁰ A familial history of the disease is exceedingly helpful in reaching a diagnosis but cannot always be obtained. The following case is presented as illustrating the difficulties that may be encountered in diagnosis; it is also of interest because of the unusual association with a severe colitis.

*From the service of Edward L. Bortz, M.D., Lankenau Hospital, Philadelphia.

ceived prior treatment with liver, have been summarized in Table 1.

The first test of red cell fragility was normal. As subsequent preoperative and postoperative tests were consistently increased, it is felt that the initial test was probably a misleading error in technic.

In retrospect, the operation was delayed too long because an enlarged spleen could not be detected. Several authors^{3, 12} have stressed the fact that the severity of the anemia in a hemolytic crisis bears no relation whatsoever to the size of the spleen.

The patient was given too many transfusions—sixteen in all—before it became apparent that they were unavailing. In this disease every transfusion is an invitation to disaster in the biliary tract.¹⁷ Perhaps the tremendously increased intestinal motility and loss of blood by bowel in this particular case prevented overloading the biliary system.

What was the relation of this patient's severe

TABLE 1
DIFFERENTIAL DIAGNOSTIC FEATURES IN CONGENITAL HEMOLYTIC
ICTERUS AND PERNICIOUS ANEMIA AFTER
TREATMENT WITH LIVER

DIAGNOSTIC FEATURES	PERNICIOUS ANEMIA	CONGENITAL HEMO- LYTIC ICTERUS
Reticulocytosis . . .	5 to 20 per cent	20 to 60 per cent
Marrow smear . . .	Normoblastic	Normoblastic
Peripheral blood smear	Marked poikilocy- tosis and slight an- isochromia	No poikilocytosis and marked anisochro- mia
Red blood cell fragility	Decreased or normal	Increased
Free gastric acid .	Always absent	May be absent
Stool and urine urobilinogen	Increased slightly	Increased greatly

colitis to her anemia? The anemia appeared first. The colitis disappeared after splenectomy cured her anemia. It is not felt that the association was accidental. The operation was delayed while attempts were made to combat her colitis, but it is now believed that this unusual complication is an even more pressing reason for immediate splenectomy.

REFERENCES

- MINKOWSKI, O.: Ueber einen hereditäre unter Bilde eines chronischen Ikterus mit Urobilinurie, Splenomegalie und Nieren siderosis verlaufende Affektion. *Verhandl. d. deutsch. Kong. f. inn. Med.* 18:316, 1900.
- DOAN, C. A., and others: The hemolytotoxic equilibrium and emergency splenectomy. *J.A.M.A.* 105:1567, 1935.
- LORD DAWSON of Penn.: Haemolytic icterus. *Brit. M. J.* 1:921, 1931.
- DAMESHEK, W., and others: Spherocytosis and increased erythrocyte fragility as indicators of hemolytic activity. *J. Clin. Investigation* 18:479, 1939.
- DAMESHEK, W., and SCHWARTZ, S. O.: Acute hemolytic anemia. *Medicine* 19:231, 1940.
- DAMESHEK, W., and MILLER, E. B.: Pathogenic mechanisms in hemolytic anemia. *Arch. Int. Med.* 72:1, 1943.
- DAMESHEK, W.: The management of acute hemolytic anemia and the hemolytic crisis. *Clinics* 2:118, 1943.
- DAMESHEK, W., and others: Hematologic changes following splenectomy in man with particular reference to target cells, hemolytic index and lysocellin. *Am. J. M. Sc.* 90:171, 1941.
- BOORMAN, K. E., and others: Haemolytic icterus, congenital and acquired. *Lancet* 1:812, 1946.
- CHIAUFFARD, A.: Pathogenic de l'ictère congénitale de l'adulte. *Semaine med.* 27:25, 1907.
- DOUTHWAITE, A. H., and WATERFIELD, R. L.: Resistant anemia. *Brit. M. J.* 1:519, 1946.
- EVANS, R. S.: Acute hemolytic anemia with autoagglutination: a case report. *Stanford M. Bull.* 1:178, 1943.
- MASON, V. R.: Acute hemolytic anemias of unknown etiology. *Tr. A. Am. Physicians* 57:234, 1942.
- MASON, V. R.: Acquired hemolytic anemia. *Arch. Int. Med.* 72:471, 1943.
- DACE, J. V.: Familial hemolytic anemia with particular reference to changes in fragility produced by splenectomy. *Quart. J. Med.* 12:101, 1943.
- VAUGHAN, J. M.: Red cell characteristics in acholuric jaundice. *J. Path. & Bact.* 45:561, 1937.
- McLAUGHLIN, C. W., JR.: Familial hemolytic jaundice, a study of results of surgical treatment. *Surgery* 12:419, 1942.
- DAVIS, L. J.: Hemolytic anemias. *Edinburgh M. J.* 50:589, 1943.
- BRANCH, C. D.: Congenital hemolytic jaundice. *Illinois M. J.* 8:235, 1941.
- STRAGNEL, R., and SMITH, K.: Congenital hemolytic jaundice in a negro family. *Am. J. Med.* 1:53, 1946.
- EISENBERG, L. H., and BROWN, J. R.: Splenectomy in familial hemolytic jaundice. *Am. J. Surg.* 72:179, 1946.
- WHIPPLE, A. O.: Recent studies in circulation of the portal bed and spleen in relation to splenomegaly. *Tr. & Stud. Coll. Physicians, Philadelphia* 8:203, 1941.
- HURLEY, A. G., and MOORE, W. C.: Congenital hemolytic jaundice. *Ann. Surg.* 112:393, 1940.
- MANDELBAUM, H.: Congenital hemolytic jaundice: report of a case: initial hemolytic crisis occurring at age 75: splenectomy followed by recovery. *Ann. Int. Med.* 13:872, 1939.
- HEDGECOCK, E. B., and PATTERSON, S. M.: Congenital hemolytic anemia. *Clinics* 1:1021, 1943.
- HADLEY, R. L.: The mechanism of the increased fragility of the erythrocytes in congenital hemolytic jaundice. *Am. J. M. Sc.* 188:441, 1934.
- SHARP, J. C.: Hemolytic jaundice: a clinical analysis of 28 cases. *Ann. Int. Med.* 14:953, 1940.

The basal metabolic rate was plus 21 per cent. An electrocardiograph was normal.

She was given 1 cc. of reticulogen daily for ten days with slight improvement in her anemia. After two weeks the patient refused further studies and treatment and left the hospital against advice. She was signed out as anemia, type undetermined.

Second admission—Three weeks later she was readmitted to the hospital. The physical examination did not show any significant changes, except the loss of 6 pounds. She stated that she had had a severe watery diarrhea with from 10 to 12 stools daily for the six days prior to her second admission.

At the time of this second admission the patient's red blood count was 670,000 with 20 per cent hemoglobin. The red cells showed marked anisochromia but practically no poikilocytosis. The white blood count was 33,000 with 67 per cent neutrophils. There was a 46 per cent reticulocytosis. An icterus index was 15. The indirect van den Bergh test was 2 mg. per 100 cc. The red cell fragility test was repeated and showed hemolysis beginning at 0.64 and complete at 0.40 per cent salt solution (control, 0.40 to 0.28 per cent). A smear of the sternal marrow showed a normoblastic type of red cell regeneration together with hyperplasia of the granulocytic series.

She ran an irregularly febrile course with temperature elevations to 104° F. Her profuse diarrhea failed to respond to various medications. She then averaged about 15 stools daily, many of which were grossly bloody. Repeated stool examinations were negative for typhoid, paratyphoid, and dysentery organisms. Neither ova nor parasites could be found. No splenomegaly could be detected on physical examination by many different observers. The spleen could not be visualized by x-ray. At one time the white blood count rose to 50,000, but no leukemic cells were found. The urine urobilinogen was positive in 1/10 dilution. The stool urobilinogen was 50 mg. in twenty-four hours. Repeated tests showed a persistently increased red cell fragility.

On the thirty-fifth hospital day it was decided that splenectomy presented the only

hope of cure, despite the absence of splenomegaly and jaundice. She was prepared for operation by daily transfusions for one week, which brought her red cell count to 3,000,000.

At operation the spleen was found to be enlarged. It weighed 400 gm. and measured 14 by 9 by 4.5 cm. There was a tiny accessory spleen. The biliary tract seemed normal. The colon was grossly thickened and strikingly injected throughout. Microscopically, the splenic pulp was uniformly engorged with red cells. The sinusoids varied; many were empty; some were crowded with red cells. There was a large amount of hemosiderin in the macrophages of the pulp and sinusoids.

Following the operation no further transfusions were given. The red cell count slowly rose to 4,000,000, with 78 per cent hemoglobin. The reticulocyte count fell to 1 per cent. The red cell fragility remained increased at approximately the preoperative figures. Her diarrhea slowly subsided over a period of four weeks. At present, one year after operation, she has one or sometimes two stools a day. She has gained 30 pounds. She is well and active.

DISCUSSION

This patient's past history demonstrates once again the futility and danger of treating anemia with liver and iron without making an accurate diagnosis.

Initially, the apparent picture of a macrocytic anemia was confusing. The large cells, of course, were reticulocytes. Actual measurement of the cells showed that approximately 35 per cent were microcytes. As Douthwaite and Waterfield¹¹ have emphasized, a blood smear which shows extreme variation in the size of erythrocytes without variation in shape, in the presence of a high reticulocytosis, is practically diagnostic of this disease and rules out pernicious anemia in which great variation in shape is seen. Initial confusion with pernicious anemia is so frequently reported that the principal diagnostic features, which will serve to differentiate these two diseases, when the patient has re-

ceived prior treatment with liver, have been summarized in Table 1.

The first test of red cell fragility was normal. As subsequent preoperative and postoperative tests were consistently increased, it is felt that the initial test was probably a misleading error in technic.

In retrospect, the operation was delayed too long because an enlarged spleen could not be detected. Several authors^{3, 12} have stressed the fact that the severity of the anemia in a hemolytic crisis bears no relation whatsoever to the size of the spleen.

The patient was given too many transfusions—sixteen in all—before it became apparent that they were unavailing. In this disease every transfusion is an invitation to disaster in the biliary tract.¹⁷ Perhaps the tremendously increased intestinal motility and loss of blood by bowel in this particular case prevented overloading the biliary system.

What was the relation of this patient's severe

TABLE 1
DIFFERENTIAL DIAGNOSTIC FEATURES IN CONGENITAL HEMOLYTIC
ICTERUS AND PERNICIOUS ANEMIA AFTER
TREATMENT WITH LIVER

DIAGNOSTIC FEATURES	PERNICIOUS ANEMIA	CONGENITAL HEMO- LYTIC ICTERUS
Reticulocytosis	5 to 20 per cent	20 to 60 per cent
Marrow smear	Normoblastic	Normoblastic
Peripheral blood smear	Marked poikilocy- tosis and slight an- isochromia	No poikilocytosis and marked anisochro- mia
Red blood cell fragility	Decreased or normal	Increased
Free gastric acid . . .	Always absent	May be absent
Stool and urine urobilinogen	Increased slightly	Increased greatly

colitis to her anemia? The anemia appeared first. The colitis disappeared after splenectomy cured her anemia. It is not felt that the association was accidental. The operation was delayed while attempts were made to combat her colitis, but it is now believed that this unusual complication is an even more pressing reason for immediate splenectomy.

REFERENCES

1. MINKOWSKI, O.: Ueber einem hereditäre unter Bilde eines chronischen Icterus mit Urobilinurie, Splenomegalie und Nieren sidoses verlaufende Affection. Verhandl. d. deutsch. Kong. f. inn. Med. 18:316, 1900.
2. DOAN, C. A., and others: The hemotopoietic equilibrium and emergency splenectomy. J.A.M.A. 105:1567, 1935.
3. LORD DAWSON of Penn.: Haemolytic icterus. Brit. M. J. 1:921, 1931.
4. DAMESIEK, W., and others: Spherocytosis and increased erythrocyte fragility as indicators of hemolytic activity. J. Clin. Investigation 18:479, 1939.
5. DAMESIEK, W., and SCHWARTZ, S. O.: Acute hemolytic anemia. Medicine 19:231, 1940.
6. DAMESIEK, W., and MILLER, E. B.: Pathogenic mechanisms in hemolytic anemia. Arch. Int. Med. 72:11, 1943.
7. DAMESIEK, W.: The management of acute hemolytic anemia and the hemolytic crisis. Clinics 2:118, 1943.
8. DAMESIEK, W., and others: Hematologic changes following splenectomy in man with particular reference to target cells, hemolytic index and lysolecithin. Am. J. M. Sc. 202:171, 1941.
9. BOORMAN, K. E., and others: Haemolytic icterus, congenital and acquired. Lancet 1:812, 1946.
10. CHAUFFARD, A.: Pathogenie de l'ictère congenitale de l'adulte. Semaine med. 27:25, 1907.
11. DOUTHWAITE, A. H., and WATERFIELD, R. L.: Resistant anemia. Brit. M. J. 1:1519, 1946.
12. EVANS, R. S.: Acute hemolytic anemia with autoagglutination: a case report. Stanford M. Bull. 1:178, 1943.
13. MASON, V. R.: Acute hemolytic anemias of unknown etiology. Tr. A. Am. Physicians 57:234, 1942.
14. MASON, V. R.: Acquired hemolytic anemia. Arch. Int. Med. 72:471, 1943.
15. DACIE, J. V.: Familial hemolytic anemia with particular reference to changes in fragility produced by splenectomy. Quart. J. Med. 12:101, 1943.
16. VAUGHAN, J. M.: Red cell characteristics in acholuric jaundice. J. Path. & Bact. 45:561, 1937.
17. McLAUGHLIN, C. W., JR.: Familial hemolytic jaundice: a study of results of surgical treatment. Surgery 12:410, 1942.
18. DAVIS, L. J.: Hemolytic anemias. Edinburgh M. J. 50:580, 1943.
19. BRANCH, C. D.: Congenital hemolytic jaundice. Illinois M. J. 8:235, 1941.
20. STRAGNEL, R., and SMITH, K.: Congenital hemolytic jaundice in a negro family. Am. J. Med. 1:53, 1946.
21. EISENDORF, L. H., and BROWN, J. R.: Splenectomy in familial hemolytic jaundice. Am. J. Surg. 72:179, 1946.
22. WHIPPLE, A. O.: Recent studies in circulation of the portal bed and spleen in relation to splenomegaly. Tr. & Stud. Coll. Physicians, Philadelphia 8:203, 1941.
23. HURLEY, A. G., and MOORE, W. C.: Congenital hemolytic jaundice. Ann. Surg. 112:393, 1940.
24. MANDELBAUM, H.: Congenital hemolytic jaundice: report of a case: initial hemolytic crisis occurring at age 75: splenectomy followed by recovery. Ann. Int. Med. 13:872, 1939.
25. HUDOCK, E. B., and PATTERSON, S. M.: Congenital hemolytic anemia. Clinics 1:1021, 1943.
26. HADEN, R. L.: The mechanism of the increased fragility of the erythrocytes in congenital hemolytic jaundice. Am. J. M. Sc. 188:441, 1934.
27. SHARPE, J. C.: Hemolytic jaundice: a clinical analysis of 28 cases. Ann. Int. Med. 14:952, 1940.



The Medical Bookman

DIAGNOSIS IN DAILY PRACTICE*

THE PRACTICING physician is primarily responsible for the management of those illnesses which are the major causes of disability and death. He likewise should hold himself accountable for the prompt recognition and handling of the predisabling phases of such diseases in order to prevent more drastic complications." . . . This is the opening paragraph of the preface to this newest of books on differential diagnosis in medical practice and it states compactly the purpose for which it was written.

Most authorities agree that the decline of the general practitioner, the family doctor of revered memory, is the greatest disaster in the history of modern medicine. But they also agree that the practitioner of tomorrow must be a different person from his often inadequately educated predecessor of the days of simpler living.

To be an effective doctor today, a wide general knowledge is demanded, but medical knowledge has become so complex that no doctor can hope to be familiar with all phases of it. What he should know is how to obtain the information necessary to make an early diagnosis, and with enough certainty to treat the patient before the disease has progressed too far, or be able to realize the need for specialist care when it arises. When more general physicians possess that knowledge, less patients will go to specialists in the first place, and medicine will become more efficient and less expensive.

One way to accomplish this aim is, of course, to make every doctor train himself to the competence of an internist, something which is not likely to

happen. The other way is to streamline diagnostic studies and make easily available the detailed knowledge which an internist should possess. This end can well be accomplished by Dr. White's and Dr. Geshickter's book and, as such, it is an important contribution to medical practice.

While there are something more than 2,000 recognized disease entities, thus immeasurably complicating the diagnosis of obscure symptoms, tables of mortality and morbidity in the United States show that only about 200 of them constitute 98 per cent of the conditions requiring the attention of physicians. Therefore, the authors state: "In order to determine the most valuable diagnostic procedures for routine use, statistical surveys of the leading causes of death and disability in the United States have been utilized. Abnormalities which are essential to the recognition of these prevalent diseases have been used as criteria for selecting the component steps of the examination. Only the most simple and reliable means of eliciting such abnormalities have been chosen. The object has been to arrive at a routine which is comprehensive but sufficiently brief to be employed in everyday practice. In the authors' hands, with technical help for the six laboratory procedures, the examination has been performed routinely within a period of twenty minutes."

A major departure in this book is the presence of two tables, conveniently placed on the inside of the front and back covers. The front table lists the 200 most common disease states, keyed to the text pages covering their symptoms. Inside the back pages is a list of major abnormalities usually encountered in the medical study, again keyed to appropriate tables in the text which list the disease

**Diagnosis in Daily Practice, An Office Routine Based on the Incidence of Various Diseases.* By Benjamin V. White, M.D., and Charles F. Geshickter, M.D. Philadelphia: J. B. Lippincott Company, 1947. Price: \$15.00.



EYE-STRAIN
OCULAR MUSCULAR IMBALANCE



MIGRAINE
HERPES ZOSTER
TEMPORAL ENDARTERITIS



GLAUCOMA
SUPRA-ORBITAL NEURALGIA
HISTAMINE HEADACHE



SOMATIC MANIFESTATION OF TENSION
CERVICAL MYOSITIS



MIGRAINE



CERVICAL ARTHRITIS
POSTAURICULAR NEURALGIA
POSTERIOR CERVICAL ADENITIS



TRIGEMINAL NEURALGIA



SINUSITIS



FEVERS
TOXIC STATES

Illustrations from: Diagnosis in Daily Practice

Figure 29. Common sites and leading causes of headache.

conditions in which the corresponding symptoms are present. The reader thus has available at a glance an index of both symptoms and diseases.

The most striking contribution of *Diagnosis In*

Daily Practice is the concept of "presymptomatic medicine." As the authors state: "Presymptomatic medicine lies midway between preventive medicine and therapeutic medicine. It aims at the recog-

nition or discovery of abnormalities of structure or function which may form the basis of subsequent disability or disease which cannot be eliminated by existing sanitation or hygienic measures. It is a phase of medicine which could not have existed a century ago, but has been made possible by newly acquired knowledge of the precursors or early stages of disease whose association with the fully developed form was not previously recognized.

"One of the reasons why statistical data regarding the major diseases has been neglected by the medical profession is found in the clinical approach. The practitioner must be prepared to discover and treat the ailment of the individual, regardless of its rarity, and for this reason, medical schools have laid a disproportionate emphasis upon rare diseases or those which present unusual diagnostic difficulties. In a standard textbook of medicine the major groups of diseases which are responsible for 98 per cent of the illness in the United States receive only 40 per cent of the space, and in a standard work on laboratory diagnosis the essential laboratory procedures which are applicable to the routine diagnosis of this major group comprise less than 5 per cent of the text. Thus in his medical education the future practitioner spends most of his time learning to diagnose those conditions which he will see the least number of times. The apparent assumption is that he will be forced to learn the common conditions from personal experience. The late stages in which most of the fatal diseases are diagnosed prove that this is an unwarranted assumption."

The "Diagnostic Survey," as described above, consists of: "(1) taking the past history and that of the present illness, (2) performing the physical examination, and (3) conducting an essential group of laboratory determinations."

"A survey of the approximately 200 diseases which are responsible for 98 per cent of the illness in the United States reveals that there are 16 common symptoms, 23 leading physical abnormalities, and 6 essential laboratory findings which will serve as keys to their differential diagnosis. It is entirely practical to construct the diagnostic survey around this list, since the presence or absence of any of the major diseases can be determined from them, provided a limited number of additional proce-

dures are carried out when indicated to confirm the diagnosis thus arrived at."

GOING still further, the authors list in order of their importance in causing morbidity, eight major "etiologic disease groups." These are: "(1) susceptibility to *infection with microorganisms*, (2) *degenerative changes*, (3) *exposure to trauma or adverse conditions*, (4) *metabolic and nutritional disturbances*, (5) *allergic response*, (6) *inadequacy of the adaptive function of the personality*, (7) *disturbances in the regenerative capacity of component tissues*, and (8) *congenital or acquired anomalies*."

In the matter of history taking, always the most important part of a diagnostic survey, the authors consider first the "etiologic history," which seeks the following abnormalities: "weakness; loss or gain of weight; a discharge of blood or pus; fever, chills, or sweats; uneasiness or worry; inability to get along with others."

Next is the "regional history" which elicits the following abnormalities: "headache; fainting, coma, or convulsions; earache or tinnitus; sneezing or nasal drip; sore throat; cough or shortness of breath; chest or precordial pain; dyspepsia or indigestion; change of bowel habits; cramps or abdominal soreness; menstrual disturbances; frequency or nocturia; lameness or backache; itching or rash."

Two tables then correlate symptoms and findings with regional and etiologic significance, locating them with relationship to the organs involved.

The examination procedures of the routine diagnostic survey are carried out according to a definite schedule as listed. With the complexity of modern instruments of precision, it is encouraging that the authors have placed emphasis once again upon the fundamental portions of the examination which can be carried out with little equipment except the senses of the physician. General inspection, for example, largely a lost art, should elicit the presence or the absence of: "discolored or altered complexion; cutaneous sores or blemishes; stiffness, impaired motion or posture; hoarseness; unsteadiness, ataxia, tremors, or twitches; paralysis; vasomotor instability."

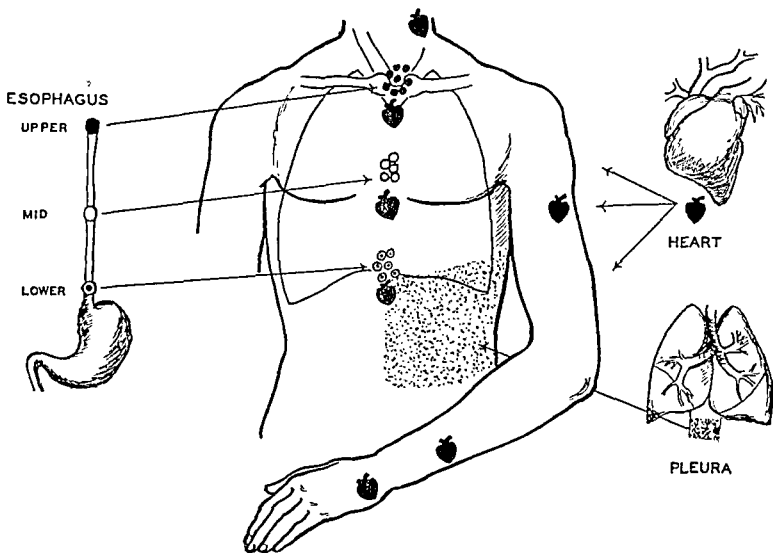


Figure 30. Thoracic regions to which cardiac, pleural and digestive pain may be referred.

Next the authors point out that: "Through the use of simple office implements, such as scales, blood pressure apparatus, stethoscope, a tongue depressor, and a good artificial light, he (the physician) is able to establish or rule out the following abnormalities: fever, loss or gain of weight; pulse or blood pressure variations; cardiac murmurs; dental abnormalities; inflamed or abnormal mucous membranes; râles, rubs, or squeaks (at the lung bases or over the precordium)."

Palpation of the neck, abdomen, and extremities notes: "masses or tenderness; edema; impaired motion or posture not noted on inspection; vascular abnormalities."

Pelvic and rectal examination yields data on: "inflamed or abnormal mucous membranes; masses or tenderness; displaced or relaxed structures."

The neurologic examination, very much simplified, brings out: "hyperreflexia or hyporeflexia; paralysis, defective vision; defective hearing." A simple psychiatric examination completes the survey with information relative to: "retarded, accelerated or bizarre animation; abnormal emotional response; fixed ideas; suspiciousness or spread of meaning; forgetfulness or disorientation."

The six laboratory procedures included in the routine diagnostic survey are: "routine examination of the urine; hemoglobin concentration of the blood; blood sedimentation rate; Mazzini serologic reaction for syphilis; occult blood in fecal material, obtained on glove by rectal examination; x-ray examination of the chest."

With the information of the survey at hand, the diagnostician can now refer to an ingenious chart

included in the book which channels positive findings to the correct disease category, and is then cross indexed to descriptions of individual diseases to be used as a final check.

The authors emphasize particularly one side of the diagnostic study which has heretofore been generally neglected, evaluation of the influence of personality upon physical symptoms. The findings of psychosomatic studies show more and more the importance of these factors. Nor is an emotional evaluation very difficult to obtain, as the authors point out, for "the ability to get along with others at home, at work, or in games or other forms of social intercourse is one of the most reliable indications of a normal personality." A simple question as to how the patient liked school will often give the clue to serious personality disturbances. Another important symptom is uneasiness or worry. These of course occur in normal individuals, but are usually not unduly prolonged. When they are, they usually mean a fundamentally unstable personality, as the authors point out, and such tension is manifested by a fairly definite physical picture which can usually be recognized.

The whole of Part II of *Diagnosis In Daily Practice* is concerned with the importance of individual symptoms in arriving at a diagnosis, including the differentiation of the several disease states presenting each symptom. Headache, for example, is listed as a symptom referable to the head, along with "fainting, coma or convulsions, and earache." It is further divided into extracranial and intracranial headache. Extracranial causes are: "optic headache, sinus headache, and cervical headache," each of which is described in full with diagnostic implications. Under intracranial headache is listed: "headache of intracranial traction or displacement; histamine and fever headaches; migraine headaches; hypertensive headache; and neurotic headache."

UNDER "Cardiorespiratory Symptoms," as a further example of the way in which etiologic factors are determined from symptoms, we find a discussion of precordial pain:

"Because of the danger in borderline psychoneurotic patients of establishing hypochondriacal tendencies referred to the heart, these data should

be acquired as far as possible from the history volunteered by the patient. In general, when substernal or precordial pain occurs in paroxysms the differential diagnosis lies between cardiovascular disease, somatic manifestations of tension, and digestive disorders; when it is chronic or persistent, one thinks of a mediastinal mass."

Part III is concerned with "Diagnostic Abnormalities of Disease: Physical Findings." Here are discussed the various findings of the physical examination. Of inspection the authors say: "The examination of the patient should bring to light objective findings regardless of whether or not their presence or significance has attracted the attention of the patient. It is often the disclosure of apparently insignificant changes, such as petechial hemorrhages of the skin or collateral circulation in the veins of the abdominal wall, which establishes the diagnosis of a major condition such as endocarditis or hepatic cirrhosis. Moreover, the incipient stages of major diseases may thus be recognized and effectively treated before disabling symptoms or irreversible changes have taken place."

In the discussion of skin diseases there are unusually clear charts of location of rashes and their characteristics on several pages of the text, materially aiding the differentiation of these conditions for the practitioner who is not always familiar with them. There are also several excellent plates in color. Other charts of external deformities of diagnostic significance, such as those of the hands, are extremely valuable.

Throughout this book, the proper place of the personality as a controlling factor in much of the symptomatology and complaints of human illness is stressed. Part III closes with the discussion of the psychiatric examination in which the authors say: "An evaluation of the behavior and personality of the patient during routine examinations to rule out psychiatric abnormalities must be accomplished by methods which are brief, unobtrusive, and relatively reliable in the hands of the practitioner who is without special training in psychiatry." An entire chapter is devoted to the psychiatric history and examination, with an evaluation of findings.

Part IV deals with the six routine laboratory examinations. Part V is concerned with differential diagnosis of the major disease groups mentioned

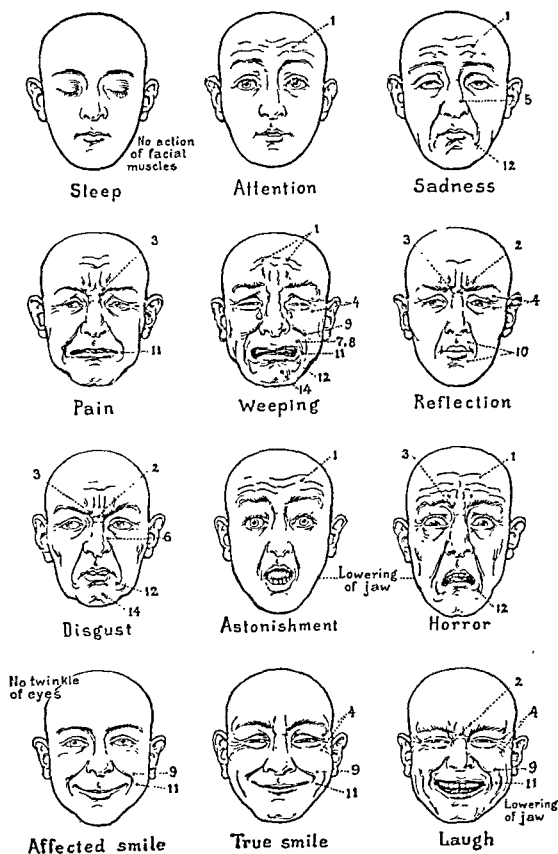


Figure 157. Facial expressions in various emotional states. From time of early infancy the child is influenced by approval or disapproval reflected in his parents' facial expressions. (From Moore, D. T. V.: *Dynamic Psychology*. Ed. 2. Philadelphia: J. B. Lippincott Company.)

earlier in the text. There are concise but complete chapters on all phases of diagnosis in all organ systems. A final chapter details the set-up of an efficiently operating office.

This is a very complete book on physical diagnosis for the general physician, bringing him in readily available form the information necessary to make a certain diagnosis in most of the conditions he will encounter. It is well written, very well organized, and has a fresh and interesting point

of view. The survey outlined here will enable the physician to practice better medicine and give his patients more complete care. In this respect it will do much to accomplish an end devoutly to be desired, the elevation of the general practitioner to a high level of competence, establishing him in his key position in the organization of medical practice. For this, if for nothing else, it is a very important and valuable book.

F. G. S.

MEN OF MEDICINE

Man of Awards

DESPITE his youth and a serious handicap, Dr. Dilworth Wayne Woolley, an associate member of the Rockefeller Institute for Medical Research, has already contributed so much to the knowledge of human nutrition that on April 12 in Havana, Cuba, he received from the American Pharmaceutical Manufacturers' Association its highest honor—the Research Award for 1948.

This tribute to the 33-year-old scientist, who is totally blind, was the first by the A.P.M.A. since the Pharmaceutical Medical Research Foundation was organized recently. The Foundation, financed chiefly by the pharmaceutical group, was announced last December by Dr. Morris Fishbein, who described it as the first project ever launched to effect a formal union of the pharmaceutical industry and the medical profession in the service of public health.

Dr. Woolley had scarcely won his doctorate from the University of Wisconsin when he lost his sight nine years ago. Thus, his blindness occurred just as he was crossing the threshold of a career which since then has placed him in the foremost ranks of the nation's physiologists.

Quietly responsive, yet unable to conceal the scientist's traditional distaste for publicity, Dr. Woolley explained that, even in the earliest days of his blindness, it had never for a moment interrupted the nutritional research which has claimed so much of his time ever since. "I just kept on going," he said laconically.

The Canadian-born scientist explained that he entrusts all laboratory routine to two assistants. These report to him their observations and from step-by-step reports Dr. Woolley controls his experiments, makes his deductions, gauges future procedure, and strikes his conclusions. In this way he pursued the research which has made him one

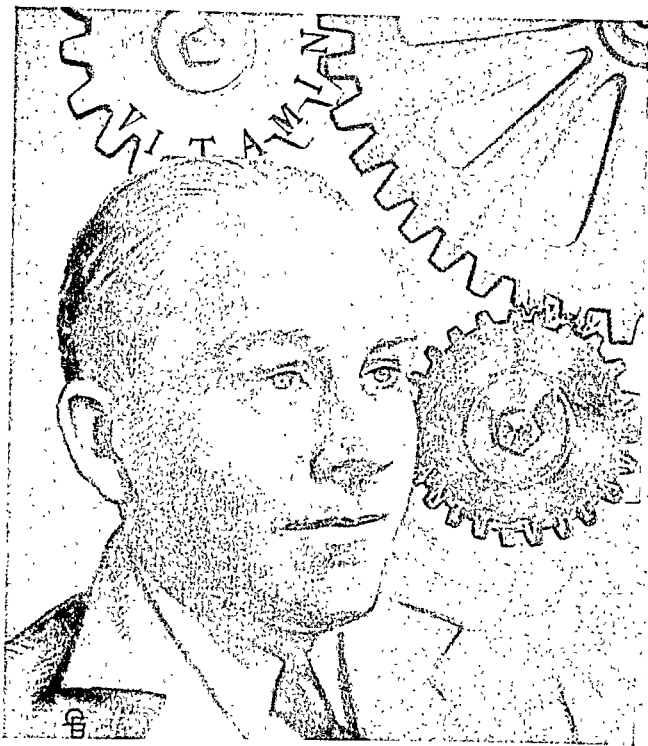
of the nation's few authorities on antimetabolites.

Dr. Woolley was born in Raymond, Alberta, and attended grammar and high schools there. Immediately after graduation from the high school, he began to specialize in the chemical-biology field at the University of Alberta, from which he graduated in 1935. He then enrolled in the graduate school of the University of Wisconsin and while still a student there published with a colleague, reports on two noteworthy experiments. These studies, completed before Dr. Woolley was 21 years old, were entitled, "The Chemistry of Mold Tissue" and "Synthetic Fats, The Preparation of Trinodecylin" respectively, and were published in the *Journal of the American Chemical Society*.

After Dr. Woolley received his doctorate from the University of Wisconsin in 1938, he spent the summer in England on a traveling fellowship of the sixteenth International Physiological Congress. In 1939 he went to the Rockefeller Institute for Medical Research (physiology) as a Fellow. In 1943 he advanced to an Associate's status at this Institute, and in 1946 became an Associate Member of the Institute.

Mrs. Woolley, the former Janet McCarter, is a bacteriologist and one of her husband's first co-authors. She also received her master's and doctor's degrees at Wisconsin. They met, worked together, and published their joint paper at that university, where the future Mrs. Woolley stayed until 1944. Then a Guggenheim Fellowship brought her to the College of Physicians and Surgeons of Columbia University. In 1945, at the completion of the fellowship, Columbia lost a bacteriologist and Woolley gained a wife who still, in Woolley's words, "shoots a guinea pig now and then" between her household duties.

DILWORTH WAYNE
WOOLLEY, Ph.D.



(Drawn by Frances O'Brien
and reproduced courtesy of
*Chemical and Engineering
News*.)

IN PRESENTING the Award to Dr. Woolley, Dr. Ernest H. Volwiler, executive vice president of Abbott Laboratories, said:

"The Research Award of the American Pharmaceutical Manufacturers' Association is the highest honor which this organization has to bestow. It is thus a valued privilege to speak of the work of a man who has so outstandingly merited and won this recognition. . . .

"In the years at Wisconsin, while he was a graduate student and for a year thereafter, Dr. Woolley's workmanship in the old laboratory in the basement of the biochemistry building at Madison became a campus legend. Some twenty contri-

butions to the literature ensued, many of them of outstanding importance and all bearing the stamp of deep, original and precise thinking.

"During these years Woolley gravitated between his original job—the chemistry of mold tissue—and the newly discovered factors of the vitamin B-complex, which were exciting the nutritionists on the floors above him. He managed to isolate the amino acids leucine, isoleucine, arginine, histidine and lysine, as well as cyclic choline sulfate from mold tissue of *Aspergillus Sydowi*. He had a hand in the isolation and characterization of nicotinic acid amide as the anti-black tongue factor and the synthesis of many compounds of related nature.



Dr. Dilworth Wayne Woolley (in dark suit) receiving the Research Award of the American Pharmaceutical Manufacturers' Association at its convention in Havana, Cuba, April 1948. Presenting the award is Dr. E. H. Volwiler, executive vice president, Abbott Laboratories, North Chicago, Ill. At the far right is James L. Rogers, retiring president of the Association and also president of the Central Pharmacal Co., Seymour, Ind. To Dr. Woolley's left is Mrs. Woolley.

He also isolated uracil from liver. Possibly his most unique and imaginative contribution while at Wisconsin, however, was his partial synthesis of pantothenic acid before the nature of this compound was even known.

"Woolley knew from the work of Williams' group at Texas that beta-alanine made up part of the molecule of the active compound and had deduced certain knowledge about the remainder of the molecule. He proceeded to acid hydrolyze a concentrate of material known to be active for chicks to completely destroy the activity. He then treated the inactive material, which appeared as just a dark brown smear, with sulfonyl chloride hoping to form an acyl chloride of the unknown fragment. He coupled this with synthetic beta-alanine. His hunch was right and he obtained again an active compound. This work helped open the way to characterization of pantothenic acid, even though

the compound was never isolated from natural sources.

"On going to Rockefeller Institute in 1939, Woolley entered into work both with various microbial strains and with rats and mice. He found inositol to be a dietary requirement for mice and used microorganisms to assay for it in foods. He found a new factor for hemolytic streptococci and identified it with a factor required for the best growth of young rats—and called it strepögenin. He determined that vitamin K is a growth factor for *Johnes' bacillus*, a study carried out with Miss Janet McCarter, while still in Madison. This experiment is noteworthy. The research team of Woolley and McCarter apparently cooperated very well and it wasn't long after Woolley went to New York that he returned to Madison to marry Miss McCarter.

"Characteristic of Woolley's thoroughness was

his follow through on inositol to show it as a constituent of a brain phosphatide (with Folch), and his isolation of lipositol, a new inositol-containing phospholipid of soy beans.

"Work with the enzyme in raw fish which destroys thiamine, and with avidin, the factor in egg-white which binds biotin, paved the way for one of Woolley's major fields of contributions to research thinking—the concept of vitamin antagonists. In rapid order Woolley developed antimetabolites for thiamine (pyrithiamine), ascorbic acid (glucoascorbic acid), nicotinic acid (3-acetyl pyridine), and vitamin K (2,3-dichloro, 4-naphthoquinone) to name only part of the list. These compounds were not only synthesized but were tested critically by Woolley, during which time he wrote four major reviews on the subject.

"The possibility for study of vitamin function is amazingly enhanced by the availability of these interesting compounds which compete with the vitamins for position in the enzyme molecule, and thereby block normal body functions. This method provides the most rational approach to the development of new chemotherapeutic agents. Woolley's work, together with his lucid and provocative writings, have had great impact in this field.

"It has been said, 'It is the intuition of unity amid diversity which impels research.' Woolley's bringing together of biochemistry, microbiology, nutrition, and organic chemistry on common grounds has been truly remarkable in providing tools and technics for research which has made for unity in our knowledge of all biology.

"Dr. Woolley, you began as a young man to add to our fund of scientific knowledge, and your contributions have risen at an accelerated rate. You have explored and solved some of our most difficult and basic problems related to nutrition and growth. It is most appropriate that this Association, dedicated to the betterment of human health, should honor itself by bestowing upon you this annual Research Award."

SPEAKING ON "The Development and Uses of Antimetabolites," Dr. Woolley described several chemical compounds which are very closely related in structure to various vitamins and hormones. "These compounds or antimetabolites," he

said, "have the power to call forth in diverse types of living things the signs of deficiency of the metabolite (i.e., vitamin or hormone) to which they are related in structure. Thus, for example, a specific slight alteration in the molecular constitution of vitamin B₁ or thiamine produces an anti-thiamine which will cause all the signs of thiamine deficiency when it is fed to animals. Other living things such as bacteria or fungi likewise can be made to develop this vitamin deficiency by giving them this antimetabolite.

"For each of the water-soluble vitamins and for several hormones and other metabolically important compounds, series of such drugs have been produced which are antagonistic to the metabolite in question.

"The mechanism by means of which these new drugs are able to produce their specific effects is viewed as a competition between the drug and the metabolite for a specific protein in the organism. Grossly, it may be likened to the introduction of a plugged nickel into a slot machine, or to the insertion of a slightly misfit key into a lock. The misfit key enters the keyhole readily but cannot quite turn the lock, and at the same time prevents the proper key from doing so.

"The knowledge gained by use of these antimetabolites has enabled the experimenter to develop new kinds of pharmacologic agents which have properties different from existing drugs. It has also allowed the successful prediction of the first members of new series of pharmacological agents; these have powers not possessed by existing drugs. At the same time an insight into the manner in which some drugs produce their effects on living things has been gained." Dr. Woolley discussed a few examples to show how these principles have been applied in experimental models and expressed the hope that these models will be of use in the future development of pharmacology and biochemistry.

In addition to the A.P.M.A. award, Dr. Woolley received an Eli Lilly award in 1940 for work in immunology and bacteriology, has been honored with the Bronze Medal from the Society of American Bacteriologists and the Mead Johnson Award in Nutrition, and will be presented with the Eli Lilly Award in Biochemistry at the 1948 fall meeting of the American Chemical Society.



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EDITORIALS

RADIATION AND THE GENERAL PHYSICIAN

IT is now more than fifty years since the discovery of the biologic effects of roentgen rays and radium and these modalities have now taken their deserved place in the treatment of properly selected benign and malignant lesions. A considerable amount of education is still needed, however, to acquaint those physicians not specializing in radiology with some facts regarding the use of these agents.

It is common knowledge that for the treatment of hematopoietic lesions, such as malignant lymphoma, leukemia, polycythemia, *et cetera*, radiation is the best palliative measure. It is not as generally understood, however, that proper irradiation of other lesions, such as primary carcinoma of the lip, is as good as surgical measures. For the care of the operable metastatic nodes from such a lesion, however, surgery appears to be far superior.

For the metastatic lesion that cannot be removed completely by surgery, a combination of surgical exposure and irradiation by interstitial radium needles or radon seeds with or without supplementary roentgen radiation will give good results in a significant number of cases. It should also be remembered that for malignant lesions of the tongue, buccal mucosa, pharynx, and palate, irradiation is ordinarily better than surgery, especially cases which are advanced.

The use of roentgen rays is also assuming its proper place in the treatment of carefully selected cases of carcinoma of the larynx. With the exception of malignant lymphoma, there is at present no place for the use of radiation

curatively in neoplasms of the lungs and gastrointestinal tract. Aside from Wilms' tumor of the kidney, occurring in children, we have no proof that irradiation benefits malignant tumors of the urinary tract, although it still appears justifiable to treat these lesions of the kidney and bladder in the adult preoperatively.

Regarding the genital tract in women, however, the story is different. For about the past thirty years the mainstay in the treatment of carcinoma of the cervix uteri has been a combination of roentgen and radium radiation and with gradual modification in technic, the five year salvage has risen to approximately 50 per cent in large groups of unselected cases.

Recent reports of the results of surgical treatment of the early stages of cervical carcinoma suggest that this method should supersede irradiation in the early and in the moderately advanced cases.

However, the reported results are not superior to those obtained by proper irradiation in comparable groups and there is the disadvantage that because of improper selection of cases many ill-advised operations are being and will be done on patients with advanced carcinoma. Many times the chances of the patient's obtaining a good result are thus materially lessened.

It is important, therefore, that there be a clarification in the thinking relative to the treatment of carcinoma of the cervix and care taken to avoid undermining confidence in irradiation for this condition. Further dissemination of the idea that surgery can supplant irradiation for this disease would be a definite step backwards.

For other malignant lesions of the female genital tract, however, surgery is the mainstay

of treatment, although it appears evident that irradiation is a valuable ancillary method, especially in the treatment of carcinoma of the uterine fundus and of the ovary. For conditions that can be adequately treated by either surgery or irradiation, it is important to remember that good irradiation is always better than poor surgery and that the converse is also true.

Physicians who are not constantly using irradiation or referring patients for this method of treatment are prone to forget that it is a major procedure when used against malignant neoplasms and that sequelae may appear early or late. The erythema, vesiculation, and superficial ulceration that follow intensive treatment of, say carcinoma of the larynx, is not properly considered an "x-ray burn" because that term by popular and legal concept denotes changes due to ignorance or neglect—and these changes will have been produced purposely.

Late roentgen damage may also appear in the form of fracture of the femoral neck, stricture of the bowel, or sloughing of the laryngeal cartilages when they are invaded by neoplasms.

It is hoped that there will be a decreasing tendency on the part of the profession generally to attribute to the irradiation all untoward symptoms which follow this procedure when given by an experienced radiologist. Sequelae are justified, however, when the treatment is given for the implacable foe—cancer. None of these changes should occur when benign lesions are treated.

In order to use roentgen rays and radium intelligently, therefore, an adequate period of specialized training and experience is required.

Fever is rarely a result of irradiation, but nausea is not uncommon when irradiation is given over the abdomen and pelvis. Transient swelling is a common concomitant of irradiation and this must be kept in mind constantly when the treatment is given over an intact cranium or masses which are causing obstruction to the air passages. But all too frequently the nonradiologic physician is prone to attribute to radiation all symptoms which he cannot otherwise easily explain. The writer has seen cases of fever blamed on radiation when the

physician *thought* the patient was being treated, but where no radiation had been given and other cases where cutaneous changes due to the repeated application of a hot water bottle were attributed to irradiation and called an "x-ray burn"—when no radiation had been given over the area.

To say, of course, that no unjustified damage is done by radiation would be false, but so is unjustified damage done by poorly advised and poorly performed surgical operations. It is important to remember that each method—radiation and surgery—is important in the treatment of malignant neoplasms, that they are complementary and not competitive, and that an appreciation of the advantage of each in various conditions must be honestly sought by all who care for cancer.

H. D. K.

THE "ALLERGY SEASON"

THE transition period from summer to fall has always been a very difficult one for the allergic patient and the allergist.

Among the reasons for this may be included such factors as: the change from an outdoor life to an indoor one; the starting of heater fires, stirring up dust that has been gathering in the pipes and ducts of the furnace all summer; the change of temperature—each day the patient must adjust himself to cool, damp mornings, warm noontime and again cool, damp evenings. Usually, at this time of the year, the first wave of respiratory infection has begun—and this, in addition, adds to the difficulty of the allergic patient.

Also, a great many of these individuals have been through a pollen season during which they have not been too successfully treated. They were under-dosed or over-dosed or had no treatment at all, or were uncooperative in taking proper care of themselves. All of these conditions add to the difficulties of the patient.



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Usually this transition period lasts about two weeks. Last year was an extremely difficult one because of its great length. The ragweed pollen season was practically over about September 18. By this time, the pollen count had dropped to less than 25 and everything should have been all right. However, from September 18 to November 15, we experienced the most difficult fall season in twenty years. More severe asthma was seen (Philadelphia) during this period than ever before. Those patients suffering with sea-

sonal or non-seasonal allergic rhinitis were miserable. Patients who had been discharged as cured, who had had no trouble for several years, had a recurrence of their symptoms. Even dermatologic allergies seemed to be aggravated.

Allergists from New York and Boston reported similar experiences.

Perhaps this editorial will be provocative of suggestions that will enable us to deal better with this seasonal difficulty.

H. L. R.

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Leaves from a Doctor's Diary

By MAURICE CHIDECKEL

June 1 . . . From young Dr. Govans: "Look, a check for five thousand dollars. From that California man whose girl with bacterial endocarditis and patent ductus arteriosus I successfully treated with penicillin. Now I am going to be married. When we return from our honeymoon I want you to visit us, but come when I am in." Today the couple came back. So did the check.

June 2 . . . "Raw eggs," I told Mr. Paul Ingle, "have no deleterious effect on people with duodenal ulcer. You have not, what doctors call, an allergic response, hence you need not eliminate raw eggs from your diet. I wanted to tell you this last night when I saw you going out of the movies with your wife." "With my wife," he repeated. "Beautiful woman, isn't she? Now, please, I beg of you, don't tell my wife that you saw me with her. I have special reasons for it. Promise?"

June 3 . . . The perpetual conflict of loyalties. Grace Kenneth loves Jerome and she also loves Buddie. Jerome is the husband and Buddie is the dog. Buddie is a newcomer. The lady was unconcerned about the various forms of human allergy, atopic or nonatopic, in allergens being atopic, and the emanations from animals, in this case from beloved Buddie, causing Jerome's serious case of asthma.

There lay Buddie and growled, and there sat Jerome and wheezed, and there sat Jerome and wheezed, wheezed pitifully. "Give or drive the dog away, or hand him over to the dog pound," I advised. "What did you say?" Her eyes spat fire. "Say that again." She was in a furious mood and I lost her as a patient and a friend. I was remind-

ed of a "poem" from *Farm Festivals*, published in 1881:

*Careful with fire is a good advice
we know;
Careful with words, is ten times
doubly so.
Thoughts unexpressed may some-
times fall back dead;
But God himself can't kill them
when they're said.*



Was this a question that transcends human intelligence? A dog and a husband. Who shall it be? But then something happened. Dog and husband both went out. The husband to breathe, the dog to chase a cat. Then she heard the screeching of wheels and a sudden stop. Grace paled to transparency. She ran to the window. She feared it was the dog who was killed.

It was.

Well, she found cheer in her sister's giving birth to a new baby, the seventh. I told the little boy downstairs that he has a new brother. "Where are you running?" I asked him. "To tell mother," he informed me, "she'll be so glad."

June 6 . . . It was a turbulent land, that home of Mr. and Mrs. Wheeler, with the two combatants charging in all directions. How de-

ceptively serene the living room and its occupants looked when you entered it. He believed in the standardization of life; she abhorred inertia. He wanted children; in her opinion, there are already too many brats. He viewed all men as equals. Her hatred of foreigners, especially Greeks, was an obsession bordering on the abnormal. She viewed all Greeks as the apple vendor a few blocks away who charged 2 cents for one apple and demanded 5 cents for two. A Greek family of considerable intelligence moved in next door, and her blind intolerance became more vehement.

Today I was hastily summoned to see her. She was the textbook case of hysteria. The emotional conflict translated itself into physical disability. A few hours ago she learned that her mother's present husband was not her father; that her mother's first husband, her real father, now dead, was a Greek. The contractures and epileptic attacks resembled organic lesions. A greater calamity could not have befallen her. To cure her is to remove the cause. How?

Can narrowness be widened? Can senseless prejudices be converted into broad tolerance? Prejudices and animosities against race, religion, foreigners. Incurable as the metastases of malignancy; unconquerable as death. That scourge will never be banished from the earth. Adroitness, persuasion, argumentation, sermons in the churches, lectures in the universities, like the moving finger in Omar Khayyam, will not erase one iota from a darkened brain. How can I eradicate the underlying cause that ages of attempted enlightenment failed, and cure the disease that is prevalent in the cultured and the enlightened?

And as I sat and thought and pondered and reflected, there was a tap on my shoulder. Mr. Khasanowitch wanted a bit of information. The urologist learned that he has five hundred dollars and advised immediate operation on his prostate gland. He wanted to know: "Suppose I would not have five hundred dollars, would I still need to have an operation?"

June 10 . . . Middle-aged celibate colleague Hugh Hill's life became nothing but that of inner emptiness. His thoughts did not lend themselves to rhetorical expression, or to no expression at all. The trained and disciplined temper common, or supposedly common, to all medical practitioners, failed him. He was robbed of his sweetheart, and he brought her over to the robber.

The bad man: aged 46, suffering from the commonest disease transmitted from animal to man, brucellosis. The disease, chronic, was now elusive and difficult to treat. He established the diagnosis by the agglutination test, and he considered it final. The patient, a very wealthy bachelor, after years of ill health, was now wholly incapacitated. Dr. Hill is a poor man and his bride-to-be, Thelma Darling, is no richer. The doctor persuaded the young woman to nurse him twenty-four hours a day, until. Thelma Darling found the helpless man very interesting. I entered the doctor's office as he was reading a little book called *The Psychology of Rumor* in which the authors state that it is impossible to exercise scientific control on genuine rumors.



"Rumor," spoke Dr. Hill, "is meaningless. There is a rumor in the neighborhood that Thelma is infatuated with Austin Kenny, that crippled creature. You know what a monstrous falsehood that is."

Two days later he learned that

the rumor was a bodied fact, for Thelma married Mr. Kenny. The epithets the doctor applied to both could be found in no dictionary. Those who have known the pulsing excitement of love will understand the wounds inflicted on brother Hill. But praised be the Lord. In His great and infinite mercy He called His suffering son, Austin, unto Himself, and so liberated Thelma Darling from the bonds of matrimony. Today, yes today, one week after Austin's death, Dr. Hill and nurse Darling became fused into one. "Do you think my nursing hastened his relief?" she spoke and laughed heartily. Could be. Anyhow life for my colleague is no longer empty. It is once more momentous and full of meaning, and of money.

* * *

June 15 . . . No member of the medical profession can be accused of infirmity of mind, or of mind's inactivity. Creative thought is a part of it, and this thought created the unionization idea. Ah, a Doctor's Union. This union will lift the profession out of servility, will eradicate all legitimate grievances, will prevent one doctor's stealing a patient from another doctor, will force the patient to pay his bills, will force the admitting offices in the hospital to do away with favoritism, and many other benefits. And won't we have a host of exciting experiences. If our demands are not granted, we will have a sit-down strike. We will just sit.

What will we demand? That's beside the point. . . . We have union, we must make demands. Shall we join the C.I.O., the A.F.L., or be a separate entity? I propose a separate entity. We must be original. As men of science we cannot, we must not, be content with imitative effort. We must be careful in selecting our officers. No man living is fit to be trusted with unlimited powers. A name? The Association of Physicians and Surgeons of the American Continent sounds im-

pressive. This appellation would include urologists, psychologists, gynecologists, pathologists, cardiologists, allergists, dermatologists, phthisiologists, obstetricians, pediatricians, diagnosticians (no technicians), radiologists, microscopists, ophthalmologists, and what have you.

The status of the stragglers of the vanishing tribe, the general practitioners, like myself, will have to be decided at a special meeting. Shall they be admitted as equals? Preposterous. A motion will be made to change the name from general practitioner to medical brokers. Of course there will be divisions and subdivisions, and so many locals. Division of Gynecology, local No. 898, department of Leukorrhea; Division of Obstetrics, local 3009, department of Sterility in the Female. Same division, local 310, department of Neonatal Salvage. Division of Pediatrics, department of Prevention of Diaper Rash, and so on, and so on, and so more on.

Maybe we can get John Lewis to help us organize a strike, and a sympathy strike from dentists, pharmacists, veterinary surgeons, and chiropractors. A strike, a sit-down strike is always thrilling. Does this appeal to you, brother healer?

Now is there such a thing as stealing a patient? Is the patient your private property, doctor, and hasn't he a right to choose any physician he trusts? Isn't it better to unite, as we did until now, for the advancement of the science of medicine and for the betterment of the human race? Let the patient be your pal, not just a piece of merchandise; establish a human relationship between your patient and yourself, and never, I say never, overcharge. No one can give you what he hasn't got.

The last two sentences I spoke aloud to myself. From the next room came the voice of my redheaded wife: "Look who is talking."

* * *

The Association Between Gastric Achlorhydria and Subacute Combined Degeneration of the Spinal Cord

TOM D. SPIES,¹ ROBERT E. STONE,² GUILLERMO GARCIA LOPEZ,³
FERNANDO MILANES,⁴ TOMAS ARAMBURU,⁵ AND RUBEN LOPEZ TOCA⁶

NORTHWESTERN UNIVERSITY, CHICAGO, AND UNIVERSITY OF HAVANA, CUBA

IT HAS long been recognized that persons with pernicious anemia have an imperfect secretion of gastric juice. As early as 1870, Fenwick¹ stressed the possibility of an important relationship between the gastric secretions and blood formation. Castle and his associates² have done a great deal to establish experimentally the nature of the abnormality in gastric function and the anti-anemic substances stored in the liver. The cause of the gastric dysfunction *per se*, however, is not elucidated. Pernicious anemia often occurs in several members of a family and frequently in succeeding generations, but whether this dysfunction is congenital or is an acquired defect has not been conclusively settled. The disease usually occurs late in life.

¹Professor of Nutrition and Metabolism and Chairman of the Department, Northwestern University, Chicago, Illinois.

²Associate Director, Nutrition Clinic, Birmingham, Alabama.

³Associate Professor of General Pathology, University of Havana, Havana, Cuba.

⁴Associate Professor of General Pathology, University of Havana, Havana, Cuba.

⁵Williams-Waterman Fellow in Nutrition.

⁶Rockefeller Fellow in Nutrition.

This study was supported by a grant from Lederle Laboratories, Inc.

Northwestern University Studies in Nutrition at the Hillman Hospital, Birmingham, Alabama, and at the Calixto Garcia Hospital, Havana, Cuba.

From the Department of Nutrition and Metabolism, Northwestern University and the Department of General Pathology, University of Havana.

Whatever may be the pathogenesis of the anemia and the gastric dysfunction, it has long been recognized that there is an association between neural degeneration and pernicious anemia. Leichtenstern³ in 1884 published an account of 3 patients with pernicious anemia in whom "tabes dorsalis" was present. In 1893 Nonne⁴ discussed the association of neural degeneration and pernicious anemia. Recently, Rundles⁵ has reviewed the more modern aspects of subacute combined degeneration. The anemia usually precedes the neural disturbances although neural disturbances may occur without any blood changes and it is well known that the extent of the neural involvement is not directly dependent on the degree of anemia present.

In recent years it has become increasingly clear that there are a number of types of macrocytic anemia that will respond to liver extract. It now has become widely accepted that folic acid is an anti-anemic factor which stimulates the bone marrow of persons with Addisonian pernicious anemia, nutritional macrocytic anemia, and the macrocytic anemia of pellagra, pregnancy, and sprue.⁶ It is abundantly clear that folic acid neither prevents subacute combined degeneration nor cures it once it has developed.⁶⁻¹¹ The present study, which has ex-



TOM D. SPIES

tended over two years, is concerned with efforts to determine in advance the susceptibility to subacute degeneration of the spinal cord in persons with macrocytic anemia and with gastric achlorhydria in contrast to persons with macrocytic anemia without gastric achlorhydria, once they are started on folic acid therapy.

MATERIAL AND METHODS

ONE hundred and sixty adult patients* with macrocytic anemia were selected in Birmingham, Alabama, and in Havana, Cuba, using the following basic criteria: (a) a color index of 1 or more; (b) a red blood cell count of 2,500,000 or less; (c) megaloblastic arrest of the sternal bone marrow; (d) the patient must be untreated or not have been treated recently enough to interfere with the evaluation of anti-anemic therapy; and (e) the patient must have

*Four patients with aleukemic leukemia, 3 with aplastic anemia, and 4 who could not be classified to the satisfaction of all observers were not included in this series although they were studied intensively.

no evidence of subacute combined degeneration of the spinal cord.

These patients were then classified as to the type of anemia. Group 1 included 37 cases in Birmingham and 1 case in Havana who had a histamine refractory achlorhydria on repeated gastric analyses† who were tentatively diagnosed as Addisonian pernicious anemia. (Not included in this series were 4 other patients in the Havana group who had no free hydrochloric acid in the gastric contents after histamine stimulation. These patients had acid steatorrhea and a long history of "sprue-like" symptoms. They responded promptly and fully to folic acid and are now in good health and will not be discussed further in this report.)

Group 2 included 13 cases in Birmingham and 18 in Havana who had free hydrochloric acid in the gastric secretions after histamine stimulation and evidence of concomitant nutritive failure, who were tentatively diagnosed as nutritional macrocytic anemia. (We see a relatively small number of patients with nutritional macrocytic anemia and sprue who have no free acid after histamine stimulation who change after treatment and have free acid, but this is not usually the case.)

Group 3 included 5 pregnant women in Havana who had typical macrocytic anemia without other complications who were diagnosed as the macrocytic anemia of pregnancy.

Group 4 included 82 patients in Havana who were diagnosed as having tropical sprue. These patients had free hydrochloric acid and enzymes in the gastric secretion after histamine stimulation; a flat curve after a single oral dose of glucose; glossitis; diarrhea characterized by steatorrhea, and a weight loss of at least 30 pounds in the six months prior to study.

The patients were admitted to the hospital where rigid dietary control was initiated and was maintained throughout the course of the

†We have found, as have many others, that some 20 per cent of the patients in the older age groups have no free hydrochloric acid in the gastric secretions after histamine stimulation but do not have anemia. Occasionally patients with histamine refractory achlorhydria developed free hydrochloric acid after treatment. Accordingly, we make only a tentative diagnosis of pernicious anemia based on the absence of free hydrochloric acid in the gastric secretions.

study. Meat, meat products, fish, poultry, milk, cheese, and eggs were excluded from the diets.

Hematologic examinations were made daily with the assistance of Mary B. Koch, Margaret H. Caldwell, Virginia Minnich, Jane Davis, Georgia Gwinner, Belle Culver, Madeline Hill, Mary Sax, Ann English, Doris Godwin, Helen Grant, and Anne Ellis. The laboratory determinations included white cell and erythrocyte counts, hemoglobin determinations, and reticulocyte counts daily. The hemoglobin content of the blood was determined in grams by means of a Leitz photoelectric colorimeter. The reticulocytes were counted in wet preparations by the use of a modified brilliant blue solution of Dameshek. Permanent fixed preparations of blood smears were made on all patients on admission and just prior to therapy and, once or twice a week thereafter, cell volumes were determined on oxalated venous blood by means of Wintrobe hematocrit tubes.

In each case, bone marrow was obtained prior to treatment by sternal aspiration using a Turkel trephine instrument for biopsies and marrow infusions—14-17 gauge, 20 mm. long. An effort was made to obtain another specimen at the peak of reticulocytosis, and still another was obtained when the reticulocytes returned to normal. Differential counts were made on preparations with both supravital and Wright-Giemsa stains. Icteric index was determined on those patients whose skin had a lemon-yellow color.

Repeated gastric analyses were performed by Dr. Aureliano Rodriguez in Havana and by Monette Springer, Alice Rogers, Frances Prudich, and Jean Brandenburg in Birmingham. The gastric contents were tested for hydrochloric acid using Toepfer's reagent. In a few special cases the presence or absence of the intrinsic factor was determined by the method of Castle on subjects known to have pernicious anemia.

Roentgenologic examinations of the gastrointestinal tract were performed on the cases in Havana by Dr. R. L. Hernandez Beguerie and on the cases in Birmingham by the staff of the

Department of Radiology, Medical College of Alabama. Samples of the stools of most of the patients with tropical sprue were studied for ova, parasites, pathogenic bacteria and occult blood, and for fat by Drs. Fernando Milanes, Arturo Curbelo, Aureliano Rodriguez, and Pedro Kouri.

Folic acid was administered to each patient orally after all the baseline determinations were made. The dosage varied from 10 to 50 mg. daily but the great majority of patients received 10 mg. daily.

OBSERVATIONS

There was a prompt hematologic response following the administration of folic acid in each of the cases included in the study. A remarkable clinical improvement paralleled the hematologic response. Each patient volunteered that he felt much stronger than he had for a long time and that the desire for food had returned. Patients who, prior to treatment, had no desire to move, began to walk about. They began eating all the food offered on the experimental diet and frequently asked for additional servings. In all the patients who had lost weight there was a prompt gain in weight. The typical hematologic response, increase in food intake, and weight gain is shown in Figure 1, both during therapy and for several months thereafter.

WITHIN two years, but usually within a few months, 27 of the 37 cases in Birmingham and the single case in Havana diagnosed as pernicious anemia developed subacute combined degeneration. Each of these patients had prompt relief from the neural disturbances following the administration of liver extract. In contrast, no evidence of subacute combined degeneration developed in any of the 13 patients in Birmingham or the 18 in Havana diagnosed as having nutritional macrocytic anemia, or in the 5 patients diagnosed as the macrocytic anemia of pregnancy and the 82 diagnosed as tropical sprue in Havana, despite the fact that



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HEMOPOIETIC RESPONSE AND WEIGHT GAIN OF A CUBAN PATIENT WITH NUTRITIONAL MACROCYTIC ANEMIA DURING THERAPY AND FOR TWO YEARS FOLLOWING THERAPY

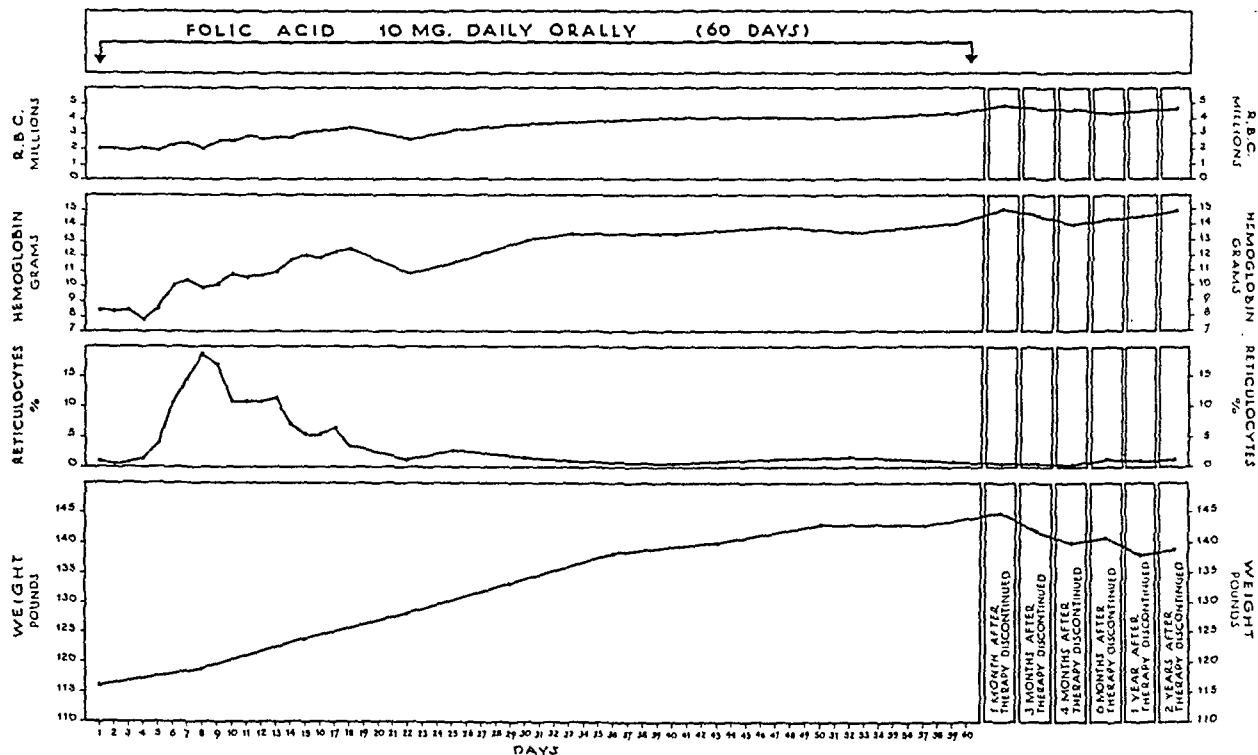


Figure 1.

they received no therapy other than folic acid.

The following case history of a patient with nutritional macrocytic anemia shows the hematologic and clinical response to folic acid therapy and the failure to develop subacute combined degeneration of the spinal cord.

Case 1—C. W., a 75-year-old white man, was admitted to the Hillman Hospital in December 1945 complaining of diarrhea, soreness of the tongue, and weakness. The family history was irrelevant.

He considered his health excellent until seven years prior to his admission when he began having infrequent bouts of diarrhea associated with cramping pains in the abdomen, anorexia, soreness of the tongue, and weakness, which usually lasted from two to three weeks and occurred chiefly during the spring and summer months. On two occasions during the preceding seven years, treatment with nicotinic acid had relieved the characteristic pel-

lagrous glossitis, the epigastric distress, and the diarrhea.

A DIETARY history revealed that as long as the patient could remember he rarely had eaten meat, eggs, milk, or fresh fruit. His diet had consisted chiefly of liberal amounts of cornbread, grits, salt pork, dried vegetables, and occasionally green vegetables. Six weeks before his admission, he began having a moderately severe watery diarrhea, cramping pains in the abdomen, and anorexia. His tongue felt thick and sore at the tip. He developed occasional cramping pains in his legs, dyspnea and cardiac palpitation on exertion. General weakness progressed and during the six-week period following the onset of his illness, he lost 13 pounds in weight.

Physical examination showed an extremely pale, well-developed man who appeared chron-

ically ill, very weak, and considerably underweight. The tongue was thick, the papillae hypertrophied, and it was abnormally red, especially at the tip. Examination of the heart, lungs, and neuromuscular system disclosed nothing remarkable.

Laboratory findings—Gastrointestinal series was negative; a barium enema showed "the sigmoid and descending portions of the colon dilated and the entire colon spastic—no filling defects." Urinalysis, Kahn blood test, and spinal fluid were negative. Gastric analysis, using Ewald's meal, showed no free hydrochloric acid in the fasting specimen, 21° and 30° of free hydrochloric acid in fifteen and twenty minutes respectively, following the test meal. The initial blood findings were: red blood cells 2,350,000, hemoglobin 9.0 gm. (50 per cent), reticulocytes 0.6 per cent. Examination of sternal bone marrow showed typical arrest at the megaloblastic level. All the observers concurred in the diagnosis of nutritional macrocytic anemia.

After baseline determinations were completed, the patient was given 10 mg. of folic acid daily by mouth. On the eighth day of therapy, the reticulocytes reached a peak of 21 per cent. By the end of the fourth week on therapy, the red blood cells numbered 3,910,000, hemoglobin 12.8 gm. (83 per cent), and reticulocytes 1.8 per cent.

ON THE third day of therapy, the patient volunteered that he was hungry for the first time in many months and he ate all the food offered on the experimental diet. The following day he asked for additional servings of food. By this time, his tongue was no longer sore and the epigastric distress had disappeared. The diarrhea gradually subsided and had disappeared by the end of a week on therapy. His strength returned and by the time he was discharged four weeks after the initiation of therapy, he had gained 15 pounds in weight. At this time, his red blood cell count was 3,910,000, hemoglobin 12.0 gm., and reticulocytes 1.8 per cent. In the two and one-half years

which have elapsed since he was discharged, he has had no recurrence of anemia or other symptoms, and frequent neurologic examinations have revealed no evidence of nerve involvement.

The following case history of a patient with Addisonian pernicious anemia illustrates the hematologic and clinical response to folic acid therapy, the subsequent development of subacute combined degeneration, and its relief following liver extract therapy.

Case 2—T. R., a 68-year-old white male cabinet maker, was first treated for pernicious anemia in 1931 by means of liver extract. At that time he was sick, had soreness of the mouth and tongue, and anorexia and dyspnea on exertion. He recovered rapidly and soon returned to work.

He occasionally ate liver and took liver extract at irregular intervals and in varying amounts with the result that he had a relapse during the summer of 1945. He took 10 mg. of folic acid daily by mouth. The initial counts were: red blood cells 1,980,000, hemoglobin 8.4 gm. (55 per cent), reticulocytes 1.0 per cent, white blood cells 3,500, and packed-cell volume 37 per cent. His blood responded well.

Symptoms related to the neuromuscular system first developed in the summer of 1946 with insidious onset of numbness of the feet, which gradually spread to the knees, and slowly increasing difficulty in walking; knee and ankle joints would give way, he would stub his toes, sway and fall. However, he stated that he worked efficiently making cabinets until about three and one-half weeks before his admission to the hospital; at that time he became disabled "overnight." There was a rapid increase in the severity of the paresthesia of the lower extremities, numbness and tingling and fleeting superficial pains of feet, legs, and lower half of the thighs; his hands felt numb and tingled for the first time; he could not walk without holding to the furniture in his room, could not step without watching where he placed his feet, and the lower extremities were hardly strong enough to support his weight.

On admission to the hospital in August 1947,

he appeared well-nourished and in no apparent distress while at rest in bed. There was very slight pallor of finger tips and conjunctivae; no icterus was noted; scalp hair was gray. The pupils were slightly irregular and reacted sluggishly to light and accommodation; hearing was moderately impaired for conversational tones; his tongue was almost smooth and the tip and margins were light red; the buccal mucosa generally was slightly hyperemic and a superficial fissure extended laterally from the right corner of his mouth externally. Heart and lungs were normal; there was slight tenderness in the lower abdomen. Anal sphincter tone was normal. The bicep reflexes were slightly hyperactive and knee jerks and ankle jerks equally hypoactive; the plantar reaction was plantar flexion; abdominal reflexes were absent.

There was no vibratory perception at the ankles and knees, very slight at the pelvis, but good at the wrists. There was slight to moderate impairment of pain and light touch sensation of feet, legs, and lower thighs, and of hands and fingers to near the wrists. Position-motion sensibility of the toes and ankles was markedly impaired. There was marked ataxia of lower extremities and very slight of the uppers; he was unable to arise to standing position alone, and could not walk without great assistance; there was slight tenderness over lower legs. The sensorium apparently was clear but he was quite easily disturbed emotionally.

A GASTRIC analysis showed no free hydrochloric acid after histamine and tests for the presence of rennin and pepsinogen were negative. The urinalysis, stool examination, and Wassermann blood test were negative; gastrointestinal x-ray study was negative.

He was given 2 cc. of refined liver extract (Reticulogen) daily for thirteen days, then 1 cc. daily thereafter for seven days. The dose was then decreased to 1 cc. per week. The patient improved rapidly on Reticulogen therapy. Despite the fact that he had some residual neurologic symptoms and physical signs, he

returned to his job as a cabinet maker eighty days after treatment was started and has continued to work each day without interruption.

In another series of three cases of Addisonian pernicious anemia, one with severe and two with mild subacute combined degeneration, we have seen remarkable improvement following the parenteral injection of vitamin B₁₂. Prior to the injection of the bright red crystals of vitamin B₁₂, each of the patients complained of pain, tingling, and stiffness in the extremities. Following the administration of 15 micrograms of this material intramuscularly to each patient, Case 1, which was acute, remarked that the numbness, tingling, and pain diminished progressively during the first ten days after the injection. Stiffness and feeling of enlargement of the joints likewise subsided and allowed the patient to walk with ease. Within two weeks, there was remarkable improvement in the clinical findings of peripheral nerve-posterior column involvement.

Case 2, which was severe, noted decreasing amounts of pain, tingling, and coldness of the extremities. Three days following the injection, her feet perspired for the first time in months. During the two weeks' time, there was slight improvement in the physical findings, though this was less definite than in the first case.

Case 3, who had chronic peripheral nerve-posterior column involvement, observed diminishing paresthesia and stiffness of the extremities which improved locomotion considerably. During the two-week interval, there were no significant objective physical changes except apparent improvement in locomotion.

The fact that three patients with achlorhydria, Addisonian pernicious anemia, and combined system disease all volunteered relief of symptoms following parenteral injection of 15 micrograms of vitamin B₁₂ is of very great interest in this regard.

SUMMARY AND CONCLUSIONS

1. A two-year study of the effect of synthetic folic acid in persons with macrocytic anemia in Birmingham, Alabama, and Havana, Cuba,

confirms and extends previous observations that folic acid is an effective anti-anemia substance capable of producing a clinical response and hematologic remission in persons with nutritional macrocytic anemia, tropical sprue, and the macrocytic anemia of pellagra and pregnancy.

2. It has long been known that subacute combined degeneration develops in persons with Addisonian pernicious anemia. This study shows that folic acid stimulates the bone marrow in this disease without preventing the neural disturbances. Twenty-eight of the 38 cases in this study who were observed over a period of two years developed subacute combined degeneration. Irrespective of how much folic acid was administered to these persons, it became worse until liver extract was administered. Following massive liver extract therapy, it was promptly relieved. In every instance in which subacute combined degeneration developed in this series, the patient had gastric achlorhydria on repeated tests following histamine stimulation, prior to folic acid therapy.

3. In contrast to the persons with Addisonian pernicious anemia, those with nutritional macrocytic anemia, tropical sprue, and the macrocytic anemia of pregnancy in this series did not have histamine refractory achlorhydria either previous to or during therapy with folic acid and in no instance did any evidence of subacute combined degeneration develop. These findings suggest an important relationship between histamine refractory achlorhydria and the development of subacute combined degeneration.

4. These findings suggest that folic acid therapy is analogous to therapy with niacin, thiamine, and other vitamins of the B complex and that its administration is effective for certain manifestations. In the eighteen years in which the senior author has been working with clinical

deficiency diseases, he has seen much evidence to support the concept that vitamin deficiency diseases in human beings tend to be multiple in nature. The administration of a specific vitamin corrects for a deficiency of itself and often aids in improving the general health and well-being of the patient but it cannot correct a deficiency of all of the essential dietary nutrients. Patients who remain on an inadequate diet and return to work tend to relapse sooner than those who remain at rest.

5. In another series of three patients with achlorhydria, Addisonian pernicious anemia, and subacute combined degeneration of the spinal cord, all volunteered relief of symptoms following the parenteral injection of 15 micrograms of vitamin B₁₂. The subjective improvement in all three patients was remarkable; and in the case which was most acute, there was considerable improvement in physical signs.

REFERENCES

1. FENWICK, S.: *Lancet* 2:78 (July 16) 1870.
2. CASTLE, W. B., HEATH, C. W., and STRAUSS, M. B.: Observations on the etiologic relationship of achylia gastrica to pernicious anemia IV. *Ann. J. M. Sc.* 182:741, 1931.
3. LEIGHTENSTERN, O.: *Deutsche med. Wchnschr.* 1884, p. 849.
4. NONNE, M.: *Arch. f. Psychiat.* 25:421, 1893.
5. RUNDLES, R. W.: Prognosis in the neurologic manifestations of pernicious anemia. *Blood* 1:209-219 (May) 1946.
6. SPIES, TOM D.: Experiences with folic acid. Chicago, The Year Book Publishers, 1947, 110 pp.
7. SPIES, TOM D., and STONE, ROBERT E.: Some recent experiences with vitamins and vitamin deficiencies. *South. M. J.* 40:46-55 (January) 1947.
8. SPIES, TOM D., and STONE, ROBERT E.: Liver extract, folic acid, and thymine in pernicious anemia and subacute combined degeneration. *Lancet* 1:174-176 (February 1) 1947.
9. VILTER, CARL F., VILTER, RICHARD W., and SPIES, TOM D.: The treatment of pernicious and related anemias with synthetic folic acid; observations on maintenance of normal hematologic status and on occurrence of combined system disease at end of one year. *J. Lab. & Clin. Med.* 32:262-273 (March) 1947.
10. HEINLE, ROBERT W., and WELCH, ARNOLD D.: Folic acid in pernicious anemia; failure to prevent neurologic relapse. *J.A.M.A.* 133:739-741 (March 15) 1947.
11. ROSS, J. F., BELDING, H., and PAEGEL, B. L.: The development and progression of subacute combined degeneration of the spinal cord with pernicious anemia treated with synthetic pteroylglutamic (folic) acid. *Blood* 3:68, 1948.



Small, Commonly Unrecognized Strokes

WALTER C. ALVAREZ*

MAYO CLINIC, ROCHESTER, MINNESOTA

ONE OF the commonest diseases of man is the slow petering-out toward the end of life, and one of the commonest reasons for such petering-out is the gradual destruction of parts of the brain by repeated thromboses of small sclerotic blood vessels. As Osler said, many persons take as long to die as they did to grow up, and they live a sort of death in life. Recently I heard of a patient who was thirty years a-dying. The process began with three apparently small strokes at the age of 57. They did not affect muscles or skin or speech, but they so crippled the man mentally that he had to retire from business. Following this, he was somewhat childish, very forgetful, and a terrible problem in his home. He lived on in this state, and died at the age of 87.

SMALL INFARCTS OF THE BRAIN ARE COMMON

As neuropathologists have pointed out, at necropsies of older persons with arteriosclerosis, one commonly finds any number of tiny infarcts in the brain. The problem is to correlate these infarcts with episodes during life.

*Division of Medicine, Mayo Clinic, Rochester, Minnesota.

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One would think that there must have been little spells of some kind, perhaps with giddiness or headache or a faint, but often the patients' physicians made no note of any such episodes. In many cases they diagnosed only acute indigestion, or a little Meniere's disease, or an upset liver.

SMALL STROKES COMMONLY GO UNRECOGNIZED

Every so often I see an older person with troubles which I think represent the residue of a little stroke partly because they came suddenly at a certain moment of a certain day. In most of these cases the history, as taken by an intern or assistant, is not good enough to reveal what actually happened; the physician must think of what might have happened and then must draw forth the typical story. Too often he does not think of a stroke, or if he does, he may dismiss the idea as preposterous. However, if he were to take an adequate history he would see that with the short fainting spell, or the spell of dizziness, or distress in the thorax or abdomen, there came a marked change in temperament and memory and ability. Perhaps after the little episode the patient was never again able to do a bit of work or to enjoy one moment of life. To me these facts are always highly significant.

THE PATIENT OFTEN GUESSES WHAT HAPPENED

OFTEN the patient realizes what happened to him even when his doctors do not. Many times I have said to a patient, "Haven't you a pretty good hunch as to what happened to you?" And the man answers, "Yes, at the time I was almost certain I was having a stroke, and that is what I now think I had." As a sweet little old lady once said, with great clearness of vision, "Death has been taking little bites of me!" She saw that with each dizzy spell, or fainting spell, or spell of confusion, or severe headache she became a little older, a little weaker, a bit more tired, her step more hesitant, her memory less trustworthy, her handwriting less legible, and her interest in life less keen. She realized that for some ten years or more she had been moving step by step toward the grave. Her doctor hooted at the idea, but *she* knew what was going on; she knew that something seriously wrong was taking place in her brain.



WALTER C. ALVAREZ

THE DISEASE AS A WHOLE HAS NOT BEEN DESCRIBED

Curiously, this common disease is almost unknown today; cases of it are never shown to medical students; articles on it are practically never read before medical societies, and when I searched through the books, journals, and the larger systems of medicine, hunting for an adequate description of this disease, I could not find one. I found, of course, descriptions of some syndromes due to cerebral arteriosclerosis, and to spasms of intracranial blood vessels, but nowhere did I find a picture of the disease as a whole—the disease which begins commonly in the forties and gradually pulls the patient down into his grave.¹

THE NEED FOR QUESTIONING RELATIVES AND FRIENDS

Often I see cases in which a man's wife and family and business associates realize that something terrible has happened to his brain; they know that he is not the fine, sensible, kindly

person that he was before he had his big dizzy spell, and they know that he can no longer carry on in his business. He has lost his drive and his judgment and his ability to get things done. Often the family physician who has known the man for years knows that he is greatly changed, and oftentimes he realizes that there must have been a stroke. It is the city consultant who commonly misses the diagnosis because he fails to draw forth the story, and depends on tests which show nothing. Furthermore, he depends on the history the patient gives him and he does not question the wife and relatives and friends who are far more likely to give him the essential information as to deterioration of character.

PHYSICIANS ARE RELUCTANT TO DIAGNOSE A STROKE

Curiously, most of us physicians hate even to mention strokes, and we hate to face the situation; we dodge it and make some other

diagnosis. Usually, we refuse to talk honestly to the patient about his real trouble. I wonder if we are still influenced by the old idea that there is something disgraceful about a stroke—that it came because God was angry with the man and struck him down. Many persons believe that. Obviously, we physicians know better; we know that all that happened was that a little artery which had become narrowed because of disease suddenly plugged up.

ONE difficulty I have had in convincing some doctors that their patient had a little stroke was my inability to convince them that the brain had been injured. They said, "But the man has no neurologic signs." My answer was that to my way of thinking a decided change in character, or a great loss of memory, or a sudden nervous breakdown, or a marked loss of interest in grooming, or a change in handwriting, or a thickening of speech, is a neurologic sign.

Another thing we physicians often do, when perhaps we admit that something went wrong in the brain, is to maintain that there was only a temporary spasm of a vessel. Although it is probable that in some cases this is true, in most cases it is not. Pathologists believe now that in most cases there was a thrombosis.

Another trouble with us physicians is that commonly we forget that the brain is an organ of the body and that it should have a lot of diseases all its own. Our peculiar training in medical school has left us without any tendency to think of the brain. If a man drops down in a faint and dies a few days later, we say he had a heart attack. He may have had, but he may also have had a vascular accident in his brain.

Perhaps the main reason why this very common disease of slow dying is not well known to the medical profession is that different physicians generally see the patient in his different episodes, and hence they do not get any idea of the disease as a whole. This can be gotten only by a physician who practices among families, or best yet, by one who has a chance to watch

the slow unrolling of the disease in some of his older relatives.

A TYPICAL CASE OF SLOW DETERIORATION

The first patient who started my study of this disease and the one who eventually caused me to recognize it in its entirety was a relative of mine, an able college president who, during the middle half of his life, had several curious nervous breakdowns. The first came at about the age of 33 years and the next about six years later. On each of these occasions he had to take a year off to recuperate. As I did not know him then, I cannot give details about his illness, but some of the able physicians who saw him then thought that the trouble was with his kidneys. A few thought he might have a smoldering tuberculosis. Subsequent events indicated that they were wrong, and what the man probably had were episodes in the course of the long disease which eventually killed him.

After he had recovered from his second sudden illness and nervous breakdown, he had to take an easier job. About two years later he had a sudden severe shock and almost died. It was thought to be a heart attack, but this is very unlikely because during the years that followed the man never showed any symptoms or signs of heart disease. Evidently he had had a good-sized stroke, because signs of deterioration in character promptly appeared. Formerly a lovable Irishman, he now became irritable and irascible. Formerly he was most careful about the cleanliness of his body and his clothes; now his wife had to insist that he bathe and change his linen. Formerly well mannered at table, he now ate coarsely. His business associates noticed the marked change in grooming and the changes in his character, and thought that he must be tippling in secret or taking some drug.

Later, he apparently had a little stroke which hit his bulb and left his swallowing mechanism so impaired that at mealtimes a little food would enter his larynx and cause much coughing. This difficulty continued until the end of

his life. By this time he was a terrible problem at home because of his unreasonableness.

A little later a wealthy friend gave him a trip to the Orient, thinking that the vacation would do him good. There he had another sudden illness, after which he didn't write to his wife for nearly two months. His physician should have noted the significance of this, because previously, when on trips, he had always written a daily letter. On his return from the trip he forgot even to express thanks to the friend who had given him the vacation. This showed a big change in character, because previously he had been so polite and gracious and so punctilious about giving thanks.

After this, the man became so careless about his clothes and appearance that he had to resign from his company. He dribbled urine so that he came to reek of ammonia. Curiously, he didn't seem to notice the odor or to feel any embarrassment about it when in company. Then, one morning, on getting out of bed, he found one leg too weak to hold him up. This passed off in an hour or two but, at last, and for the first time in his illness, the true nature of one of his episodes was suspected by his physicians. Here was something that they could give a name to. During the few years that followed, he had many more little spells and finally he died, at the age of 57, of a big stroke. He died a purely brain death, his heart and kidneys and other organs working well right up to the end.

It was only after I had watched the progress of this man's illness for years that I came to realize that the episodes were all part of one disease. Later, I watched episodes such as he had had pull down others of my relatives and friends.

ANOTHER CASE

The wife of the man whose condition I have just described began to have recognizable little strokes at the age of 57. For the first time in her life she became ill. She would get a little dizzy spell, and would then feel tired and weak. She had to cut down markedly on her

activities. For years she had had a systolic blood pressure of around 200 mm. of mercury. At the age of 59 she had a big stroke, with hemiplegia and complete aphasia. With this her weight dropped from about 190 to 100 pounds (86 to 45 kg.). Destructive changes promptly appeared in the right hip joint on the same side as that of the paralysis. Her blood pressure dropped to normal, and remained that way for the rest of her life. With this stroke she lost all her old feeling of good health; she became utterly miserable; she said she felt awful, and had lost all joy in life. Fortunately, she kept her sweet character, and many of her interests in business and family.

During the remaining six years of her life I watched her have attack after attack of dizziness, nausea and vomiting, and sometimes much mental distress; sometimes she would be prostrated in bed for a few days after one of these jolts. When she died, necropsy showed her brain to be speckled with scores of little brown infarcts. There were enough, and more, to account for all the dozens of little episodes that she had had. There was no need to invoke the idea of temporary *spasms* in blood vessels. There was no other lesion in her body to account for the long illness and death.

Naturally, these little strokes are most likely to appear in the sixties or fifties or forties, but they can be found in the thirties, and during the second World War they were observed even in soldiers in their late twenties.

PARESTHESIAS REFERRED OUT FROM THE BRAIN TO THE THORAX OR ABDOMEN

I, who am supposed to be a gastroenterologist, often see these people because a little stroke was accompanied by some sort of storm down the vagus nerves, or by a curious distress, or pain referred out into the abdomen. For instance, a physician one day suddenly felt as if something were torn in two in the abdomen. Careful studies at a hospital failed to show anything wrong, and there was no sign of shock such as there would have been if something had gone wrong in the abdomen. Later, there

was a similar episode with a similar prostration. On both occasions the patient had to stay in bed for some time because of great weakness and apathy. In many of these cases the wave of heat or distress or pain is referred into the thorax and is then mistaken for a symptom of angina pectoris.

MANY STROKES CANNOT BE RECOGNIZED AT THE TIME

Sometimes I am fairly certain that a patient's illness is due to one or more little strokes, but I cannot get a history of them. Sometimes I think I might if I could interview members of the family or the business entourage. One difficulty is that many small thromboses probably come during the night when the blood pressure is low. Then the patient may wake with "a head on him" or much of his memory gone. Other strokes, which come in the daytime, are not associated with feelings of shock and therefore are not recognized for what they are. It is interesting to note how bad a stroke a man can have without feeling any shock or pain. I have seen men fall to the floor with a bad hemiplegia, but without any feeling of shock or mental distress.

Most small strokes do not produce any of the ordinary neurologic signs of nerve or brain injury, because there are so many places in the brain in which one can put a good-sized area of destruction without producing any weakness of a muscle or any patch of anesthesia in the skin.

OFTEN I have been uncertain about the nature of a suspected episode until the patient came back two or three times with the story of some much more definite, little or big strokes. Sometimes a patient will say that he fell or slipped or stumbled or miscalculated the height of a step, but the fact that for weeks or months afterward he was a bit confused or dizzy or *off* work, makes it seem more probable was due to a slight stroke. Many so-called acute indigestion are really

DETAILS WHICH SUGGEST THAT THERE MAY HAVE BEEN A STROKE

With many a small stroke the blood pressure suddenly falls to normal. Such a fall, I think, is fairly pathognomonic of a little stroke. Sometimes the pressure goes back up, but sometimes it does not.

A sudden, inexplicable loss of weight may also be due to a little stroke. In the case of the woman whose story I have given in this paper, there was, after her big stroke, a prompt loss of about 90 pounds (41 kg.). I have commonly seen losses of 40 or 50 pounds (18 to 23 kg.).

I have already mentioned the distressing pains, paresthesias, or "heat-waves," or rending feelings that are referred out from the brain to the thorax or abdomen. Sometimes, after such a wave, there will be a spasm of the stomach so that food entering it will be rejected or will cause cramping. This spastic state may pass off in a couple of months.

Symptoms of slight bulbar paralysis must be watched for, and their significance recognized. Often a little stroke which hits the bulb will interfere with swallowing; it may produceropy saliva, or thickness in the speech.

Occasionally there will be a slight patch of anesthesia somewhere, or a little weakness of some muscle or some uncertainty in using hands or feet. Many persons say they feel top-heavy, or uncertain, or giddy. They feel that if they were to turn a corner quickly while looking up, they might fall down.

Most convincing often to me is a sudden change for the worse in the personality. For instance, a man who all his life had been a tower of strength to his family, always kindly, thoughtful, and considerate, and never for a moment complaining or thinking of himself, suddenly became a querulous invalid who could talk of nothing but his discomforts and his bowels that wouldn't move as they used to. No longer could his relatives come to him with their troubles; he had too many of his own. Later, there came a mild parkinsonian syndrome. Incidentally, such a syndrome late in life is probably often due to little strokes.

Sometimes, especially if a patient has much insanity in his family, with a little stroke there will come psychopathic changes. An older person will become suspicious of formerly adored children, or he will become penurious, or he may even do some things which are immoral. He may lose his business judgment and may dissipate his fortune. Often, after a man has fallen out of his chair or has fallen down in his office, he will no longer initiate anything, and his department will run down and the younger men in it will leave. In many cases such a patient becomes a terrible problem in the home, where his care is exceedingly difficult. He may fight with his children and his grandchildren. A woman, formerly a devoted wife and mother and grandmother, will no longer take any interest in home, husband, children, grandchildren, or friends. She may refuse to see old friends.

Occasionally, after a little stroke, a man or woman will go into an agitated depression. I remember several such women who walked the floor, wringing their hands and crying, and saying that their suffering was more than they could bear.

Rarely, there will be a sudden coming of insomnia in a person who always slept well before. More frequent is the coming of a fear of being left alone. Probably the man who has had a little stroke becomes much afraid of another, and hence will not stay alone if he can possibly help it.

Another symptom which I think is sometimes due to a little stroke is a burning or a bad taste in the mouth without any local lesions. This symptom is commonly seen in the cases of women around the age of 50.

Atypical facial pains in older arteriosclerotics may well be due to a little stroke. I remember a wealthy physician with such pain, who on several occasions had all his ganglions and much of his face on the affected side anesthetized with procaine, without experiencing the slightest diminution in the severity of his distress. This suggested that the lesion was higher up, in his brain; the man had had some little strokes before his pain came, and he even-

tually died with a series of them.

Sudden blindness occurs in some of these people, usually in one eye.

Arthritis with trophic changes may also come on suddenly in one extremity.

The attacks which probably are due to *spasm* in a small vessel are rather characteristic. A man may have an aphasia lasting for half an hour and then he will get perfectly well; he may have another one the next day and the day after that, and then he may go for a year without any more.

In diagnosing these little strokes I think the essential point often is the history of a sudden onset. Highly important also is a history of a change of character.

PROGNOSIS

THE prognosis is usually not very good if there is marked change in character. These are the tragic cases. In other cases after two or three small strokes I have seen a man or woman have to wait for fifteen or twenty years before there came another jolt.

TREATMENT

Obviously, in many cases there isn't very much that can be done in the way of treatment. Probably the best thing to do is not to allow anyone to treat the patient too much. One shouldn't deprive the person of all the pleasures of living such as eating, smoking, drinking, and walking about and visiting friends. No effort should be made to reduce the blood pressure. Theoretically, it is best for the circulation of the brain if the blood pressure remains high.

Should the person be told what is wrong? I think that usually, if one is dealing with an intelligent person, it is best to talk frankly. Often the patient knows what happened, and then he or she is bound to feel much better if the doctor talks honestly about the diagnosis and the chances of recovery or continued living.

REFERENCE

1. ALVAREZ, W. C.: Cerebral arteriosclerosis with small, commonly unrecognized apoplexies. *Geriatrics* 1:189-216 (May-June) 1946.

The Climacteric in Women and Men

AUGUST A. WERNER*

ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

THE TERM menopause, literally meaning cessation of menstrual flow, is commonly used to designate that critical period in a woman's life, more correctly spoken of as the climacteric. Menstrual pause may occur at any time during active sexual life from various causes. Disturbances of menstrual flow, such as irregularity, profuseness, scantiness, or cessation are only visible evidences that there is some disturbance of the function of the glands which control the menstrual mechanism.

Some women believe that when menstruation ceases at the climacteric, that they are through the change of life. They are mistaken, for menstruation ceases only because the ovaries do not function sufficiently to produce the endometrial changes that result in bleeding. It is the decrease or absence of ovarian function that initiates all of the difficulty, and not the absence of menstruation. The disturbance of, or the cessation of menstruation is only one of the phenomena which occur at the climacteric. It is the one sign which is objective and therefore it attracts most attention, but it is far from

being the most disturbing factor of the climacteric.

Menopause marks the end of the child-bearing period in a woman's life. The ovaries, which have been primarily responsible for the sex life of the individual, begin to lose their function and their responsiveness to stimulation by the pituitary gland, which is their activator. The pituitary gland becomes secondarily disturbed, and since the pituitary exercises stimulatory influence on other glands, such as the thyroid and the adrenals, a complex crisis, or climax, occurs.

The climacteric is further complicated by the fact that these ductless glands exercise varying degrees of influence on the two nervous systems, namely, the central or voluntary nervous system and the autonomic or involuntary nervous system. Both nervous systems are interrelated, but the autonomic nervous system is seemingly more disturbed, for it is the nervous network which controls the vital life processes of the organism, over which we have no control at all.

Among physiologic activities which are under autonomic control may be mentioned the emotions to a great extent, the sense of physical and mental well-being, the heart and the respiratory rates, the digestion of various foods,

*Assistant Professor of Internal Medicine, St. Louis University School of Medicine.

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and the marvelous chemical reactions which occur in the body and the various tissues, especially in the liver.

With disturbance of function of the ovaries and other interrelated glands and the imbalance of the nervous systems, a train of subjective symptoms occurs, which renders the patient uncomfortable and in many instances are very distressing. Perhaps most women experience some discomfort at the climacteric, but in many it is so mild as to be negligible. Others have a more severe disturbance and in these women the symptoms can be alleviated by proper treatment with estrogens.

It is important that the duration of the climacteric be stressed. The climacteric varies in duration with each individual. Some women enter the climacteric at about 38 years of age, while others do not experience difficulty until they are approximately 50 years of age; the average age is about 40.8 years.^{1,2} It must be remembered that a woman need not be of climacteric age to have all of the symptoms characteristic for the menopause. Since these symptoms are initiated by ovarian hypofunction or afuction, they will occur in castrates and younger women who have decreased function of the ovaries, regardless of age. A woman will not be free of symptoms until she develops the glandular equilibrium characteristic for the postmenopausal period.

In some women endocrine balance may occur within three to six months, while in others the imbalance may last five, six, or even more years. There are also some women who claim not to have had any appreciable disturbances at the time of cessation of menstruation, and who perhaps five to ten years later, at ages of 50 to 60 years, develop the typical symptoms of the climacteric; there may be a renewed, but unsuccessful attempt by the pituitary to stimulate gonadal function. This has been described by the author as the postmenopausal syndrome. Practically all of these women respond favorably to treatment with estrogenic hormones.

Hypoovarianism may be caused by disease conditions such as the degenerative or inflamma-

tory processes in, or adjacent to the ovaries, as inflamed tubes or appendicitis, which may cause degeneration in the glands. It may be secondary to constitutional disease processes as in certain anemias, tuberculosis, or malignancies. Vitamin deficiency in the diet may be a cause. It may be primary as in some cases in which the ovaries fail to develop or attain complete function. It may be secondary to secretory deficiency of the pituitary, as in some types of infantilism or obesity. It may occur after partial castration when one ovary has been removed or only a small part of one ovary remains. It will be complete when both ovaries are removed, unless there is accessory ovarian tissue. It always occurs at some time during the climacteric.

SYMPTOMS CHARACTERISTIC FOR OVARIAN HYPOFUNCTION, AFUNCTION, AND THE CLIMACTERIC

DISTURBANCES which accompany ovarian hypofunction and afuction and which occur, especially at the climacteric, may be divided into objective signs and subjective symptoms.¹⁻¹¹

Objective signs—The objective signs include various types of menstrual disorders occurring separately or with varying degrees of combination, such as irregularity, scantiness of flow with decreased duration (hypomenorrhea), and finally, cessation of menstruation (amenorrhea). Excessive bleeding at menstruation (menorrhagia) and profuse irregular bleeding between the menstrual periods (metrorrhagia) are more apt to occur in women who are approaching the natural menopause than in those of younger age. In castrates, the cessation of bleeding follows the operation, if all ovarian tissue has been removed.

Obesity, second objective sign, is characterized by a generalized deposition of fat, or a localized deposition over the trochanters and fatty enlargement of the breasts. The localization of fat over the trochanters and in the breasts usually occurs in younger women who have ovarian hypofunction and in castrates after they reach the age of approximately 30



AUGUST A. WERNER

years. Many obese girls, when they attain the age of puberty, have delayed, irregular, or scanty menstruation, or they may have complete absence of menstruation; this is usually due to a complex endocrine disorder.

Following the termination of pregnancy, a complicated endocrine readjustment must occur in the woman, and frequently the glands do not strike a normal balance, with the result that many women have various types of menstrual disorders and some of them date their onset of obesity from one of their pregnancies. Other signs of ovarian hypofunction or afunction are atrophy of the genitals and breasts and loss of genital and axillary hair.

Subjective symptoms—The subjective symptoms accompanying ovarian hypofunction or afunction render the patient more uncomfortable than do the objective signs. These subjective symptoms may be classified as nervous, circulatory, and general in origin. A proper evaluation of their significance is necessary as these symptoms are the chief basis of diagnosis

of ovarian hypofunction or afunction.

Subjective nervousness is an intense feeling of nervous tension. Many patients state that they feel jumpy, or trembly inside their body; a common expression is that they have "butterflies in the stomach." Some state that they feel like screaming, or as though they might lose their mind. In most instances, they do not have a tremor, but occasionally this nervousness may become so extreme as to cause some tremulousness. (Table 1.)

Excitability is a nervous state in which the persons respond to ordinary stimuli in an exaggerated manner, especially in regard to their psychic reaction. Unfavorable news, slight mishaps, arguments, all manner of little occurrences that would not disturb a normal individual cause quite a nervous and mental flurry.

These people are very irritable and easily aggravated or excited to anger by deed or word. They are hard to please. Noises of playing children, the radio, almost anything stirs them to action. In fact, they need no special stimuli; they are simply hard to get along with. In many instances they acknowledge this condition, but state that they cannot help being so.

HHEADACHES of various types and locations occur, but they are rarely migrainous. Migraine is a sick headache, usually unilateral, and may be accompanied by nausea and vomiting. When migraine occurs with endocrine disorders, it is probably only initiated or aggravated by the glandular irregularity.

The usual headaches may be described by the patient as dull to severe aches, not neuralgic in type. They may occur irregularly, or be continuous. Patients have been observed with headaches lasting continuously for thirty to forty days which were relieved by proper endocrine treatment. Their location may be temporal, frontal, or supraorbital, and there may be a sensation of retro-orbital pressure which may cause the eyes to ache.

There are two types of headaches which have almost specific diagnostic importance in hypovarianism, vertex and occipitocervical.

TABLE 1
FREQUENCY OF NERVOUS SYMPTOMS IN WOMEN

	53 Castrates Per Cent	96 Menopause Per Cent	48 Involuntal Melancholia Per Cent
Nervousness, subjective.....	100.0	92.7	100.0
Excitability.....	84.2	72.9	100.0
Irritability.....	68.0	61.4	95.8
Headache.....	36.0	50.0	83.3
Occipitocervical pain.....	58.0	37.5	56.2
Decreased memory and concentration.....	51.0	54.1	95.8
Depression, crying.....	71.7	60.4	100.0
Psychosis.....	20.8	35.4	100.0
Formication.....	23.1	23.9	29.2
Sleep disturbed.....	66.0	59.3	72.9

Patients describe the vertex ache as if a great weight were resting on the head and some state that they feel as if the top of the head wanted to push out.

Occipitocervical aching is located in the occiput and it radiates to the nape of the neck and at times over the shoulders or down the spine. It is described as a severe, dull combination of ache and pain which may be continuous for days. When this ache is present many patients say their minds are hazy or fogged.

Among nervous symptoms may be classed psychic depression, commonly called "the blues." When in this state these patients have no special interest in ordinary activities. They cannot "cheer up." It is an effort to smile or laugh, they do not want company or care to enter into pleasurable entertainment. Frequently this depression is accompanied by crying for no reason at all. They state that they cannot prevent this. This condition, if untreated or unimproved, may progress to anxiety psychosis in which the patients feel ill at ease. They have a fear of impending danger which they cannot explain. They worry unnecessarily and feel that something dreadful will happen to them, their loved ones or others. Some patients whose past life had been rather Bohemian develop an extremely religious outlook.

Decreased memory and ability for mental concentration are observed. Patients forget where they put things. They cannot remember, especially recent events. The mental processes are slow and they cerebrates slowly. The

mind seems hazy or fogged. If they read an article they cannot tell what they have read and frequently must reread it three or four times before it registers.

Formication, a sensation as if ants or insects were crawling over the skin, especially on the arms, back, and body, is complained of frequently. There also may be prickling or tingling of the skin.

A LARGE majority of these patients complain of sleeping poorly. They may be restless, sleeping only for short intervals during the night. Some fall asleep quickly upon retiring only to awaken within a half hour and remain awake for varying lengths of time. Others do not sleep upon retiring until after midnight. Some complain that they sleep well until 2 or 3 A.M. and then remain awake until morning. Patients who do not sleep at night find themselves exhausted the next day and must sleep during the daytime. This desire to sleep during the daylight hours must not be confused with somnolence.

Hot flushes have always been considered positive proof that a woman was in the menopause. (Table 2.) This is not literally true, for some patients who have many climacteric symptoms do not have hot flushes. Hot flushes are characterized by sudden redness of the face and neck, upper chest and at times, most of the body, due to a dilatation of the superficial capillaries of the skin. It is a very uncomfortable

TABLE 2
FREQUENCY OF CIRCULATORY SYMPTOMS IN WOMEN

	53 Castrates Per Cent	96 Menopause Per Cent	48 Involutional Melancholia Per Cent
Hot flushes.....	94.3	91.6	81.2
Tachycardia, palpitation, dyspnea.....	54.7	72.9	79.0
Vertigo.....	68.0	71.8	62.5
Scotomata.....	43.4	50.0	12.5
Cold hands and feet.....	43.4	23.9	81.0
Numbness, tingling.....	37.7	29.1	77.1
Pulse average per minute.....	76.	78.3	76.
Blood pressure, average.....	123/76.	138/88.6	128/76.
Pulse pressure, average.....	47.	50.	52.

able sensation and generally is of short duration, but it may last for half an hour, or even longer if the statements of some patients are correct. Frequently the flushes are described as a smothering sensation. They may be accompanied by vertigo, scotomata, or tingling or prickling sensations over the head, neck, and body. They are frequently accompanied by profuse perspiration, and the patient may feel faint. Occasionally hot flushes alternate with, or follow chilly sensations over the same areas. Hot flushes may accompany disturbances of the heart and blood vessels, especially arteriosclerosis with hypertension, but these conditions can be eliminated by proper diagnosis.

These patients notice tachycardia, palpitation and dyspnea more than usual upon moderate effort, without any disease condition to account for it. They may awake at night with tachycardia and palpitation, which usually is of short duration.

They also complain of easy fatigability; sweeping, ascending a flight of stairs, walking a block to the store, almost any moderate effort causes them to fatigue more than normally and may be associated with mild to moderate palpitation, tachycardia, and dyspnea. Patients frequently state that they are more tired upon arising in the morning than when they retired.

Vertigo with change of position and even while changing position in bed, is another very frequent symptom. It is generally more annoying than serious. Tinnitus as a buzzing, hissing, or a ringing sound in the ears is frequently complained of.

FREQUENTLY there are scotomata as dark spots or silvery specks floating before the eyes. Vertigo, tinnitus, and scotomata often occur concurrently and of these vertigo is the most frequent. Cold hands, feet, and extremities are commonly found in this condition.

The pulse rate is usually not changed much unless there is thyroid disturbance. In some instances the blood pressure may be moderately increased but this usually returns to normal with proper treatment.

General symptoms—Constipation is very frequently found in people of climacteric age, but it is probably not a condition which is directly attributable to the endocrine disturbance. In the vast majority of patients, constipation is probably due to improper habits, diet, or gastrointestinal disorders. (Table 3.)

Patients complain of vague pains and their location may be as legion as is the distribution of the sensory nerves. One of the most common pains is a boring ache which may be located below the lower angle of the scapulae or in the center of the upper part of the back. Again, it may be anywhere along the spine, especially in the lumbosacral region and the legs may ache. Pain in the chest, over the region of the heart is frequently complained of; usually this pain over the heart is in the chest wall and is not caused by any heart condition.

There is a condition known as menopausal arthritis characterized by soreness in various joints throughout the body, without redness or swelling, which may last from a few days to

TABLE 3
FREQUENCY OF GENERAL SYMPTOMS AND SIGNS IN WOMEN

	53 Castrates Per Cent	96 Menopause Per Cent	48 Involutional Melancholia Per Cent
Lassitude, fatigability.....	75.0	78.1	98.0
Constipation.....	72.5	72.9	83.3
Vague pains.....	Not recorded	Not recorded	77.1
Obesity.....	28.0	51.1	8.33
	Chiefly gonad (43 cases recorded)	Pit. and thy. (86 cases recorded*)	Moderate obesity (4 cases recorded)
Menstrual disorder.....	100.0	97.7	100.0
Amenorrhea.....	94.3	41.5	37 more than 6 mos. 11 less than 6 mos. See special reference
Basal metabolism.....	+6.4 (6 cases)	+8.2 (17 cases) -7.0 (3 cases)	

*Obese before menopause, 18; after menopause, 26.

an indefinite period. The joints most commonly involved are those of the fingers, hands, wrists, shoulders, and the spine, especially in the lower part of the back. In some instances there is some thickening of the joints in the fingers, which are painful.

CLIMACTERIC PSYCHOSIS (INVOLUTIONAL MELANCHOLIA)

Probably the first biologic urges of primitive man were what are now called instincts. Closely associated with instincts are the emotions. The emotions represent psychic responses to internal and especially to external stimuli. These responses are mediated through the central and autonomic nervous systems and hormones of the endocrine glands.

It is known that hyperfunction and hypofunction of the endocrine glands can so disturb persons emotionally that they manifest psychoses. The hormonal conflicts of pregnancy and necessary readjustments following parturition may result in profound disturbances of the personality and psychosis.

After an extended observation of a large number of patients over a period of years, having mild to extreme menopausal symptoms,

the author and associates concluded that so-called involutional melancholia is only the severest manifestation of the disturbances at this period in life. Knowing the efficacy of estrogens in relieving the distress of patients exhibiting the castrate-menopausal symptoms, we decided to treat a group of carefully controlled patients having involutional melan-

TABLE 4
SYNDROME ACCOMPANYING DEFICIENCY OR ABSENCE OF THE
OVARIAN FOLLICULAR HORMONE IN 197 CASES (53
CASTRATES, 96 MENOPAUSE, 48 INVOLUTIONAL
MELANCHOLIA)

Order of Frequency of Symptoms	Per Cent
1. Menstrual disturbances.....	99.2
2. Nervousness, subjective.....	97.6
3. Hot flushes.....	89.0
4. Excitability.....	85.7
5. Fatigability and lassitude.....	83.7
6. Depression and crying.....	77.4
7. Constipation.....	76.2
8. Irritability.....	75.1
9. Tachycardia, palpitation and dyspnea.....	68.8
10. Vertigo.....	67.4
11. Decreased memory and concentration.....	66.8
12. Sleep disturbed.....	66.1
13. Amenorrhea.....	57.6
14. Headaches.....	56.4
15. Psychosis.....	52.2
16. Occipitocervical aching.....	50.6
17. Scotomata.....	49.4
18. Numbness and tingling.....	48.3
19. Cold hands and feet.....	35.3
20. Formication.....	25.4
21. Vague pains (recorded for involutional melancholia).....	77.1

cholia by administration of estrogen. This was done over a course of several years and the results obtained in this series of experiments were gratifying and have been published. Many other reports have since appeared in various medical journals by other physicians.

THE MALE CLIMACTERIC

Both men and women have a pituitary-gonad relationship and it is well established now that men are subject to decreased function of the sex glands, just as women are, especially in later life.

In the girl at puberty the gonadotrophic hormones of the pituitary stimulate the ovaries to function, with the development of a follicle in the ovary and the production of an ovum. The cells lining the follicle produce estrogenic hormone, which in turn stimulates development of the breasts, the internal and external genitals, and the configuration of the body, which changes from that of the girl, through adolescence, to womanhood.

In the boy at puberty the gonadotrophic hormones stimulate the testicles to function. The interstitial cells are stimulated and these secrete testosterone which initiates development of the secondary sex characteristics and the other changes, as he develops from boyhood, through adolescence, to normal manhood.

The most obvious and fundamental difference which occurs as a result of this pituitary-gonad relationship in the human male and female is that the normal woman menstruates.

The menstrual cycle may be looked upon as

an extra phenomenon in the woman and not as an occurrence necessary for her sense of well-being. If the uterus is removed and the ovaries are healthy and their function is not disturbed, her pituitary-ovarian relationship will continue as it does in the man and she can and will feel perfectly normal, until the climacteric is reached.

As a result of the over-emphasis which has been placed upon the cessation of menstruation in the woman and because the man does not have this phenomenon, it was believed that the man did not have a climacteric. There is absolutely no basis for the belief that the man does not have a decrease in sex function in later life, and that he cannot have a climacteric. The climacteric does not necessarily preclude the possibility of sexual relationship, but there is a decline in libido and the ability in the man to have coitus as frequently as in earlier life. This also applies to women of climacteric age who have no more sex potency than have men of the same age; the seeming difference is only that of anatomic structure.

The author is inclined to believe, from clinical experience with male patients, that practically as many men as women experience some degree of glandular disturbance with characteristic symptoms, if the condition were recognized and provided that correct information were available.

The climacteric usually occurs later in men than in women. The average age of onset in women is about 40.8 years, and in men it occurs from approximately 45 to 55, or even 60 years of age.¹²⁻¹⁵ It must be remembered that neither the man nor the woman need to be of climacteric age to develop the typical climacteric symptoms. If at any time after the onset of gonadal function, there is a marked decrease of this function, regardless of age, the person is liable to develop the climacteric symptoms.

Decreased gonadal function in men may be primary or secondary. In primary insufficiency of the testicles, normally placed testes have never functioned to a normal degree. Second-

TABLE 5
FREQUENCY OF CIRCULATORY SYMPTOMS IN THE MALE
CLIMACTERIC

	Per Cent
Hot flushes	29.3
Chilly sensations	6.2
Sweating	17.9
Vertigo	46.5
Scotomas	26.0
Tinnitus	10.6
Numbness and tingling	43.9
Cold hands and feet	32.9
Tachycardia, palpitation and dyspnea	51.2

TABLE 6
FREQUENCY OF NERVOUS SYMPTOMS IN THE MALE
CLIMACTERIC

	Per Cent
Nervousness, subjective	90.5
Irritability	80.2
Excitability	49.0
Depression	77.2
Crying	15.3
Memory and concentration decreased	75.8
Loss of interest	55.8
Decrease in self confidence	27.1
Ill at ease	56.4
Fear of impending danger	40.6
Worry, unnecessary	33.7
Personality change, unsociable, desire to avoid crowds and company	23.8
Self accusatory	2.4
Feeling of futility	27.1
Thoughts of self destruction	7.4
Suicide attempted (2 persons)	
Psychoses (9 patients)	2.4
Sleep disturbed	59.3
Occipitocervical aching	41.9
Vertex pressure	17.5
Headache	31.8
Itching	31.8
Formication	20.5

TABLE 7
FREQUENCY OF GENERAL SYMPTOMS AND SIGNS IN THE
MALE CLIMACTERIC

	Per Cent
Fatigability and lassitude	80.2
Libido (data on 252 patients)	
Decreased or absent	
Yes	80.5
No	19.5
Potency (data on 263 patients)	
Decreased or absent	
Yes	90.1
No	9.9
Vague pains	32.9
Constipation	24.9
Obesity (moderate)	21.5
Social status:	Number
Single	42
Married	192
Widowed	19
Divorced	20
	Years
Average age of all patients	50.5
Average age of climacteric patients	53.7
Average age of hypogonadal cryptorchidic and eunuchoid patients	33.1

TABLE 8
THE MALE CLIMACTERIC SYNDROME: ORDER OF FREQUENCY OF
SYMPTOMS IN TWO HUNDRED AND SEVENTY-THREE PATIENTS

	Per Cent
1. Nervousness, subjective	90.5
2. Potency decreased or absent	90.1
3. Libido decreased or absent	80.5
4. Irritability	80.2
5. Fatigability and lassitude	80.2
6. Depression	77.2
7. Memory and concentration decreased	75.8
8. Sleep disturbed	59.3
9. Loss of interest	58.5
10. Ill at ease	56.4
11. Tachycardia, palpitation and dyspnea	51.2
12. Excitability	49.0
13. Vertigo	46.5
14. Numbness and tingling	43.9
15. Occipitocervical aching	41.9
16. Fear	40.6
17. Worry, unnecessary	33.7
18. Cold hands and feet	32.9
19. Vague pains	32.9
20. Headache	31.8
21. Itching	31.8
22. Hot flushes	29.3
23. Loss of self confidence	27.1
24. Futility	27.1
25. Scotomas	26.0
26. Constipation	24.9
27. Unsociability	23.8
28. Obesity	21.5
29. Aching in the vertex	17.5
30. Sweating	17.9
31. Crying	15.3
32. Tinnitus	10.6
33. Thoughts of self destruction	7.4
34. Chilly sensations	6.2
35. Self accusatory	2.4
36. Psychosis	2.4
37. Suicide attempted (2 patients)	

sexual life of the individual and it may result from insufficient stimulation of the testicles by the pituitary gland, or failure of adequate response of the testicles to normal stimulation by the pituitary. The testicles may be subject to decreased function following toxic conditions, infections, and various other ailments. Insufficient function of the thyroid gland is sometimes responsible for hypofunction of the testicles, by failure to stimulate normal chemical cellular activity of all body structures, including the testes.

Complete or partial loss of function of the testicles can also occur from any of the following conditions, namely, castration or bilateral inflammation of the testicles from any cause especially mumps, or following opera-

ary decreased function of the testes occurs when these glands apparently have functioned normally and later there is a decrease in their secretory activity.

Secondary failure to function normally may occur at any time during the period of active

tions for hernia, if the circulation to the testicles is markedly impaired. X-ray radiation of the male genital organs in the region of the testicles may injure these glands so that they will lose their function, if they are not properly protected. In some instances it is necessary to use the x-ray for treatment, as in malignant conditions.

If any of these harmful conditions occur after the patient has had normal gonadal function, severe glandular imbalance will result in the appearance of the symptoms characteristic of the climacteric and these symptoms may persist with varying intensity until the time for the individual to develop a normal postclimacteric endocrine balance, which may be an indefinite number of years.

AFTER a man has developed normally and functioned sexually, and then has hypofunction or afunction at some later date, the diagnostic evidence for the condition is chiefly subjective, rather than objective. The symptoms result from functional imbalance between the pituitary and the testes (the thyroid and adrenal glands may be secondarily involved), with disturbance of the autonomic and central nervous systems. The symptoms are necessarily chiefly functional. (Tables 5 to 8.)

The author made diagnostic surveys of 273 male patients, each of whom had one of the

types of testicular underactivity. Of these patients, 230 were in the climacteric, while the remainder of the patients had hypofunction or afunction, due to failure of normal development or conditions which destroyed testicular function.

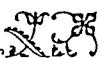


Most of these patients complained of symptoms similar in every detail to those found in the female climacteric. Nervousness, poor sleep, easy fatigue, and irritation were all found among the males. The characteristic vertex and occipital headaches, decreased concentration, and mood changes even to melancholia were significant at this time.

Men have hot flushes similar to women. Vertigo, tinnitus, lassitude, and fatigue are often present. Most of these men have noticed a decrease in sexual potency, and in many instances the decline of potency and the persistence of libido causes many men to consult the physician.

The great majority of these patients volunteered the information, that decrease of libido and potency, with few exceptions, were not their chief concern. They were more interested in having relief of their symptoms, especially those which were nervous and psychic; they wanted to feel well, so that they could work. One can almost surely promise a climacteric patient relief from his symptoms and a feeling of well-being, by treatment with the proper dosages of testosterone.

REFERENCES

1. WERNER, AUGUST A.: Syndrome accompanying ovarian hypofunction. *J. Missouri M. A.* 28:363-369, 1931.
2. ———: Syndrome accompanying deficiency or absence of ovarian follicular hormone. *Endocrinology* 19:695-700, 1935.
3. ———: *Endocrinology, clinical application and treatment*. Ed. 2. Philadelphia, Lea & Febiger, 1942.
4. ———, and COLLIER, W. D.: The effect of theelin injections on the castrated woman. *Proc. Soc. Exper. Biol. & Med.* 29:1142 (June) 1932.
5. ———, and ———: The effect of theelin injections on the castrated woman, with histologic report. *J.A.M.A.* 100:633, 1933.
6. ———, and ———: Production of endometrial growth in castrated woman. *J.A.M.A.* 101:1466, 1933.
7. ———, JONES, G., ROBERTS, J., BROUN, G. O., NEILSON, C. H., and ROTHERMICH, N. O.: Effective clinical dosages of theelin in oil. *J.A.M.A.* 109:1027, 1937.
8. ———, JOHNS, G. A., HOCTOR, E. F., AULT, C. C., KOHLER, L., and WEIS, M. W.: Involutional melancholia: probable etiology and treatment. *I. J.A.M.A.* 103:13-16, 1933.
9. ———, KOHLER, L. H., AULT, C. C., and HOCTOR, E. F.: Involutional melancholia, probable etiology and treatment. *II. Arch. Neurol. & Psychiat.* 35:1076, 1936.
10. AULT, C. C., HOCTOR, E. F., and WERNER, A. A.: Theelin therapy in the psychoses. *J.A.M.A.* 109:1786, 1937.
11. WERNER, A. A., HOCTOR, E. F., and AULT, C. C.: Involutional melancholia, a review with additional cases. *Arch. Neurol. & Psychiat.* 45:944, 1941.
12. WERNER, AUGUST A.: The male climacteric. *J.A.M.A.* 112:1441-1443 (April 15) 1939.
13. ———: The male climacteric; additional observations of thirty-seven patients. *J. Urol.* 49 (June) 1942.
14. ———: The male climacteric; report of fifty-four cases. *J.A.M.A.* 127:705-710 (March 24) 1945.
15. ———: The male climacteric; report of two hundred seventy-three cases. *J.A.M.A.* 132:188 (September) 1946.



The Treatment of Prostatic Cancer

REED M. NESBIT*

UNIVERSITY OF MICHIGAN MEDICAL SCHOOL, ANN ARBOR

NEVER before during recorded history has man enjoyed such longevity as at the present time. At the turn of the century the life expectancy in our country was 47 years; today it is 20 years greater; but with this remarkable lengthening of life there has been a corresponding increase in the number of deaths due to cancer. Today there are about 17 million males in this country who are over 50 years of age—and about 20 per cent of them have cancer of the prostate. These 3 or 4 million men will not all die of the disease, but many will; and the high incidence of this malignancy constitutes a matter of grave concern for all physicians who are charged with the responsibility of caring for middle-aged or old men.

We do not know why this neoplasm develops, but its occurrence is thought to depend upon testicular function, for eunuchs have not been known to develop it. Some investigators believe that prostatic cancer develops in conjunction with benign hypertrophy and conclude that the two conditions have a common

etiologic background. But the investigations of Moore and others tend to contradict this viewpoint, for they have shown that the incidence of prostatic malignancy is as great among men with otherwise normal glands as it is among those afflicted with benign hypertrophy; and Ravisch has shown that Jews display a remarkable immunity to prostatic carcinoma although benign enlargements do tend to occur commonly among them.

The clinical approach to the problem of prostatic cancer is concerned with three essential enterprises, prevention of the disease, its cure, and palliative or suppressive treatment when it has fully developed.

PREVENTION

In general, the prevention of prostatic cancer is not practically feasible, for nothing short of total prostatectomy can today be regarded as an absolute prophylaxis against the disease. However, total prostatectomy has been recommended for the treatment of many nonmalignant conditions today, and those urologists who routinely perform perineal prostatectomy in the treatment of benign enlargements might logically advocate total prostatectomy whenever the perineal approach is indicated, thus

*Department of Surgery, University of Michigan Hospital, Ann Arbor.

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REED M. NESBIT

adding the benefit of cancer prevention to the other advantages inherent in the perineal operation. But total prostatectomy is invariably followed by complete sexual impotence and many individuals who suffer from prostatism would be unwilling to exchange their remaining sexual powers for prevention of cancer if they knew that 4 out of 5 persons do not develop the disease anyway.

CURE

CURE of prostatic cancer can be accomplished only by radical perineal prostatectomy that is performed while the lesion is sharply localized. Every man who is found to have an area of induration in the prostate should be afforded the benefit of perineal exposure of the prostate so that frozen section biopsy can be performed, and early radical removal of the gland carried out if malignancy is present. Only in this way can cure of prostatic cancer be effected.

Most women today have been educated to the importance of periodic examinations of the breasts, but the male population in general is totally ignorant about the dangers of prostatic cancer, or of the need of periodic rectal examinations. Most early prostatic cancers are discovered not by urologists but by conscientious practitioners. Radical perineal prostatectomy is not a difficult operation to perform and it is a safe operation. Hinman has recently stated that five-year cures can be expected in at least 50 per cent of the cases. A recent review of the data relating to the patients who have been treated for cancer of the prostate in the University of Michigan Hospital since 1925 reveals the interesting fact that all of the patients who had radical perineal prostatectomy survived operation, all enjoy urinary continence, and all are alive today. But only 5 per cent of prostatic cancers are discovered early enough to permit the employment of radical surgery, a lamentable and dismally low figure considering the fact that most of the lesions could be recognized early if only an early rectal examination were made.

PALLIATIVE TREATMENT

The palliative or suppressive endocrine treatment of prostatic cancers which cannot be removed by radical surgery commenced in 1941 following the epoch-making discoveries of Charles Huggins, who in that year demonstrated a functional relationship between this disease and certain hormones. Since that time physicians have treated patients suffering from carcinoma of the prostate by the administration of estrogenic hormones and by surgical castration. The series of cases that are being reported currently from many clinics will doubtless provide a means for final evaluation of the methods that are being employed. Spectacular regression of the primary neoplasm has been observed in many of the patients, and, in some instances, complete disappearance of metastases has occurred. Some of the patients, however, have shown improvement for a short time only and a few have apparently derived no benefit

whatever from the endocrine modifications employed.

We have been following two closed series of cases at the University of Michigan Hospital since 1941. One of the series is composed of 75 patients who were treated by castration, while the other consisted of 50 cases treated by estrogens alone. At the present time these two series have been followed for approximately five and one-half years, and the survival rates shown in Table I have recently been tabulated for comparison.

TABLE 1
SURVIVAL RATES TO JULY 1947 (CLOSED SERIES)

	ORCHIECTOMY SERIES (75 CASES)	STILBESTROL SERIES (50 CASES)
Alive and symptom-free	22.7 per cent	18.0 per cent
Dead or recurrence of symptoms	78.3 per cent	82 per cent

These data suggest that the over-all survival rates in the two series are approximately the same. They also demonstrate that neither form of treatment offers assurance of prolonged remission, a fact that should be borne in mind in determining the most suitable time to inaugurate endocrine therapy. Added information on the latter point is afforded by the survival data (Table 2) on the patients who had cancer without metastases at the time that treatment was initiated.

TABLE 2
SURVIVAL RATES OF PATIENTS WITHOUT METASTASES
(CLOSED SERIES)

	ORCHIECTOMY SERIES (45 CASES)	STILBESTROL SERIES (33 CASES)
Alive and symptom-free	29 per cent	27.2 per cent
Dead or recurrence of symptoms	71 per cent	72.8 per cent

It is evident that neither form of therapy affords prophylaxis in the prevention of metastases or advance of the disease, and reason would seem to dictate that endocrine therapy be regarded as a palliative measure only, and for

TABLE 3
SURVIVAL RATES OF PATIENTS WITH METASTASES
(CLOSED SERIES)

	ORCHIECTOMY SERIES (30 CASES)	STILBESTROL SERIES (17 CASES)
Alive and symptom-free	13.3 per cent	0 per cent
Dead or recurrence of symptoms	86.6 per cent	100 per cent

that reason it should be employed only in advanced stages of the disease.

Many questions have arisen concerning the relative merits of the two methods of endocrine therapy that are under discussion. Huggins has steadfastly contended that castration is complete, and that its effects are continuous; but other observers have favored estrogen therapy in the view that this hormone neutralizes not only the testicular hormone, but also other hormones which might stimulate the growth of the tumor.

One obvious and practical disadvantage to estrogen therapy is the ever-present human attribute of forgetfulness and neglect. One-fifth of the patients in our estrogen series forgot or failed to take their pills regularly; and at least two of the patients stopped taking the hormone altogether, after having gone into a remission, in the belief that the cancer had been cured! Another disadvantage in the method of using estrogens is some of the patients who failed to respond satisfactorily to estrogen therapy have had remissions following castration, but none of the castration failures have been improved by estrogen therapy.

Additional evidence in the comparison of the two methods of endocrine therapy is afforded by the survival data on patients who had demonstrable metastases at the time treatment was begun (Table 3).

In Table 3 it would appear that orchietomy is more effective than estrogen therapy as a palliative measure in those patients with metastasis. However, when the data are subjected to statistical analysis (Chi-Square formula and Yates' correction), it is found that the differences between the orchietomy series and the

stilbestrol series are not statistically significant at the 5 per cent level in either table. That means that such differences might be expected to arise by chance more often than five times in a hundred and we can therefore make no statistical statement regarding the superiority of one treatment over the other, other factors being equal. More time is necessary and larger series of cases must be critically analyzed before final evaluations can be made, but the present series permits the inference that castration provides better clinical response than estrogen therapy alone.

CONCLUSIONS

Cancer of the prostate can be cured by early recognition and radical perineal prostatectomy, but it is to be deplored that only 5 per cent of the cases are recognized early enough to permit the operation.

Endocrine therapy is a palliative measure that is best reserved until the advanced stages of the disease have developed, and the evidence that has been presented suggests that castration may be more effective than estrogen therapy alone in producing remissions in patients suffering from advanced cancer of the prostate.

NEW FILM ON MANAGEMENT OF FAILING HEART

AFTER two years of preparation, announcement has been made of the completion of a new sound and color film entitled "Management of the Failing Heart." The new forty minute length film is available to medical groups throughout the country.

A modern regimen for the treatment of congestive heart failure is narrated and depicted. Animated charts and diagrams, clinical sequences, and pathologic specimens are used to visualize the five essential steps necessary in the management of the failing heart, viz., (1) rest, (2) diuretics, (3) salt-free diet, (4) liquid intake, and (5) digitalization.

The film thoroughly airs the controversial subject of the nature of "rest," and goes into great detail regarding control of cardiac edema through a better understanding of the proper use of mercurial diuretics, the role of salt in the cardiac diet, and the subject of a liberal water intake.

The physician is shown the efficacy of the average single dose method of digitalization and simplified maintenance by the use of the purified digitalis glycoside, Digitaline Nativelle. This is demonstrated by electrocardiograms and case history charts.

The film was prepared from a text supplied by and with the cooperation of the Department of Pharmacology, Cornell University Medical School, under a grant established by Varick Pharmacal Company, Inc.

The Present Status of Antibiotic Therapy

JOHN A. KOLMER*

TEMPLE UNIVERSITY SCHOOL OF MEDICINE, PHILADELPHIA

WHILE a large number of antibiotic agents has been produced, only penicillin, streptomycin, tyrothricin, and bacitracin are being employed at the present time for prophylaxis and treatment of disease.

Crystalline sodium G and crystalline potassium G penicillins are preferred. As dispensed in a dry state, both are highly stable at ordinary temperatures while being less toxic and less irritating than amorphous products. Solutions, however, should be kept in a refrigerator. Streptomycin is dispensed as sulfate and hydrochloride salts of the compound; also as a calcium chloride complex which, in a dry state, is highly stable at ordinary temperatures. Solutions of streptomycin, however, should likewise be kept at a low temperature.

NATURAL RESISTANCE OF BACTERIA

Different strains of any bacterium susceptible to penicillin may possess a high natural resistance to the compound. Thus, streptococci of the viridans type and anaerobic streptococci

are usually much more resistant than beta hemolytic streptococci of group A; staphylococci also vary greatly in natural resistance.

The same is true of streptomycin. Thus, some strains of *Escherichia coli* and other gram-negative bacilli may be much more resistant than usual. This has an important bearing on dosage and administration and may be responsible for treatment failures. Fortunately, however, gonococci and other organisms naturally resistant to the sulfonamide compounds are usually highly susceptible to penicillin.

Sometimes streptococci, staphylococci, and other gram-positive organisms may be found less naturally resistant to streptomycin than to penicillin *in vitro*, with the suggestion that the former may be preferred in treatment.

ACQUIRED RESISTANCE OF BACTERIA

Bacteria may also show so-called acquired resistance to penicillin or streptomycin during treatment which, likewise, has an important bearing on dosage and method of administration. This happens much more rapidly and frequently to streptomycin than to penicillin.

True acquired resistance of bacteria to these compounds, however, may not actually occur but only represent the survival or emergence

*Professor of Medicine, Temple University School of Medicine and School of Dentistry; Director, Research Institute of Cutaneous Medicine, Philadelphia.

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JOHN A. KOLMER

of naturally resistant variants of any given bacterium during treatment. In other words, these compounds may rapidly reduce or eliminate highly susceptible organisms, leaving more naturally resistant variants which are thought to be organisms of so-called acquired resistance.

Under the circumstances penicillin and streptomycin should not be used indiscriminately in the prophylaxis and treatment of disease since the survival of naturally resistant variants is of epidemiologic importance.

SYNERGISTIC OR ADDITIVE CHEMOTHERAPY

SYNERGISTIC or additive chemotherapy consists of the administration of two compounds conjointly and especially in the treatment of severe infections, including mixed infections. In some instances the therapeutic effects appear to be truly synergistic while in others, they are merely additive.

Since penicillin and streptomycin are of very

low toxicity, untoward or toxic reactions are usually no greater and may be less since smaller doses of each compound may be employed than of either alone. Furthermore, this combined therapy may prevent or reduce the incidence of so-called acquired resistance of infecting organisms.

Excellent results have been observed in the treatment of various experimental infections, like syphilis of rabbits, with penicillin, mapharsen, or bismuth; tuberculosis of guinea pigs and rats with streptomycin and the sulfone compounds; streptococcal, pneumococcal, and typhoidal infections of mice with penicillin and sulfonamide compounds; *Klebsiella pneumoniae* infections of mice with streptomycin and sulfadiazine, and anthrax of mice with penicillin and streptomycin.^{1, 2, 3}

Consequently, this combined chemotherapy is frequently indicated in the treatment of the septicemias, acute bacterial endocarditides, suppurative meningitides, bronchiectasis, pneumonias, suppurative pneumonitides, sinusitis, suppurative arthritides and compound fractures, osteomyelitis, brain abscesses, carbuncles, Ludwig's angina, erysipelas, gangrene, actinomycosis, gonorrhea and its complications, and other diseases with penicillin or streptomycin and the sulfonamide compounds. It is also worthy of clinical trial in the treatment of syphilis, especially early syphilis, with penicillin, mapharsen, or bismuth as well as in the treatment of tuberculosis with streptomycin and sulfone compounds, with particular reference to promizole.

PRINCIPLES OF ANTIBIOTIC THERAPY

Whenever possible, accurate bacteriologic diagnosis is always advisable in relation to penicillin and streptomycin therapy since the administration of these compounds is indicated only in the treatment of pure or mixed infections due to susceptible organisms. In many instances, however, the physician or surgeon is justified in making a presumptive clinical diagnosis and proceeding with penicillin or streptomycin therapy without delay.

LABORATORY tests for determining the susceptibility of organisms to penicillin or streptomycin *in vitro* are also frequently advisable or necessary as a clinical guide to dosage and administration, since infections due to strains with high natural or so-called acquired resistance require larger doses and more prolonged treatment than infections due to highly susceptible organisms.

Assays of the blood, spinal, and other body fluids for penicillin or streptomycin are likewise frequently necessary or advisable at intervals during treatment as a guide to dosage and route of administration. Effective concentrations of penicillin in the serum should be within the limits of 0.02 to 2 or more units, with a general average of about 0.15 units per cc., while effective concentrations of streptomycin vary from about 2 to 20 micrograms (units) per cc. or higher, according to the nature and severity of the infection. Otherwise, and when in doubt, dosage and methods of administration of these compounds must be based upon clinical judgment and experience alone.

Treatment should always be instituted as soon as possible and especially in acute infectious diseases in which large doses over a short period of time are to be preferred to small doses over a long period.

There are practically no contraindications to penicillin or streptomycin therapy of diseases due to susceptible organisms, except in patients possessing a high degree of natural or acquired allergic sensitization to the compounds. Under these circumstances due caution is required in dosage and administration or treatment abandoned.

Penicillin or streptomycin therapy alone is not always a substitute for adjuvant measures of sound therapeutic value, with special reference to prompt drainage or other surgical measures, blood transfusions, the administration of specific immune sera, etc., and particularly in the treatment of severe infections. Indeed, neither compound is incompatible with any drug, x-ray, or any other kind of therapy of proved or helpful value, including induced fever employed in the treatment of gonorrhea,

syphilis, etc., which appears to enhance the therapeutic activity of chemotherapeutic compounds.

CAUSES OF TREATMENT FAILURES

Treatment failures may be due to any of many causes among which may be mentioned: (1) mistaken clinical or bacteriologic diagnoses; (2) infections due to organisms possessing a high natural or so-called acquired resistance to penicillin or streptomycin; (3) doses too small, intervals of administration too long, or duration of treatment too brief; (4) overwhelmingly severe infections or too long delay in the institution of treatment; (5) localization of infections in areas inaccessible to penicillin or streptomycin; (6) inadequate surgical treatment or failure to use other adjuvant measures of helpful value, and (7) the occurrence of spontaneous new infections or superinfections with other organisms indicating the frequent need for repeated bacteriologic examinations during treatment.⁴

DOSEAGE AND ADMINISTRATION OF PENICILLIN AND STREPTOMYCIN

The dosage of penicillin and streptomycin varies from one patient to another, depending not only on the nature, severity, and location of the infection, but on age, weight, the presence or absence of septicemia, and *especially susceptibility of the infecting organism to the compound.*

Consequently, the physician or surgeon should not depend on "average doses." Treatment should be individualized, especially in severe infections, since blind adherence to average doses may result in therapeutic failures. Rather, dosage should be such as to secure and maintain blood concentrations at least 2 to 5 times higher than those to which the infecting micro-organism is susceptible *in vitro*. When unfavorable therapeutic results are observed one should redetermine the sensitivity of the organism *in vitro* and the blood concentration, and promptly increase the dosage or

otherwise alter treatment as indicated.

Infections of highly vascularized soft tissues respond to doses which may be ineffective in infections of poorly vascularized and hard tissues like bones and joints; acute and diffuse lesions usually respond more favorably than chronic localized ones.

Maximum doses are always advisable at the beginning of treatment and especially in severe infections. For this purpose penicillin may be administered by continuous intravenous or intramuscular injection and streptomycin by continuous intramuscular injection.

The urinary excretion of penicillin may be reduced with a consequent increase and prolongation of blood concentrations by the oral administration of 2 gm. sodium benzoate or 2 to 4 gm. caronamide every four hours.^{5,6} Sodium benzoate has been found less effective in enhancing the blood concentrations of streptomycin⁷ while caronamide has not been reported on in this connection.

Since the duration of treatment is likewise variable, it should be guided not only by clinical judgment but by laboratory examinations whenever possible; it is better to administer too much than too little in order to prevent relapsing infections.

Repeated bacteriologic examinations are advisable for the detection and treatment of spontaneous new infections and especially with organisms normally present in the nasopharynx.⁴

In case of necessity the laity may be trained to give intermittent intramuscular injections of penicillin or streptomycin dissolved in sterile saline solution.

Penicillin should not be given orally in the treatment of severe staphylococcal infections, subacute bacterial endocarditis, all types of meningitis, and syphilis.

THERAPEUTIC VALUE OF PENICILLIN

Penicillin, with or without synergistic or adjuvant therapy, has usually proved highly effective in the treatment of various and diverse staphylococcal, streptococcal, pneumococcal, meningococcal, gonococcal, and clostridial in-

fections including postoperative bacterial synergistic gangrene. It has also proved effective in the treatment of anthrax, erysipeloid and Haverhill fever, syphilis, yaws, spirofusillar infections, and actinomycosis.

In subacute bacterial endocarditis large doses should be given over a period of at least four to eight weeks; coincident anticoagulant therapy with heparin or dicumarol may slightly improve the results but is generally regarded as too hazardous.

In primary syphilis the total dosage should be at least 6,000,000 units and at least 9,000,000 units in early secondary syphilis. In neurosyphilis, concomitant fever therapy should be employed.

Intrathecal injections should always be given at least once or twice daily in suppurative meningitis in conjunction with parenteral injections. Likewise, intrathoracic injections at least once daily in empyema and intraabdominal injections at least once daily in peritonitis with retention of the compound for at least six to eight hours in either case.

Topical applications of penicillin ointment may have to be stopped after five consecutive days because of allergic sensitization, especially in skin diseases.

THERAPEUTIC VALUE OF STREPTOMYCIN

STREPTOMYCIN is usually highly effective in treatment of tularemia, the septicemias, endocarditides, meningitides, pneumonias, and unobstructed urinary tract infections due to the pathogenic *gram-negative bacilli*.

It is of helpful or variable value in the treatment of empyema, peritonitis, liver abscess, cholangitis, wounds, burns, and compound fractures due to infections with gram-negative bacilli. Streptomycin is also of value as a suppressive agent in the treatment of exudative pulmonary tuberculosis, in tuberculous laryngitis, meningitis, peritonitis, fistulae, osteomyelitis, and arthritis, but usually ineffective in the treatment of tuberculous empyema. The compound, however, is of but doubtful value or disappointing in the treatment of acute

brucellosis, typhoid fever, paratyphoid fever, and other Salmonella infections.

Intrathecal injections of 50 to 100 mg. daily or every other day, are essential in addition to intramuscular injections in the treatment of meningitis; also intrathoracic or intraabdominal injections of 0.5 to 1.0 gm. with retention for six to eight hours in the treatment of empyema and peritonitis.

Oral administration is indicated only in preoperative preparation for intestinal surgery. Aerosols may be employed. Suspensions in peanut oil and beeswax are probably ineffective.⁸

PROPHYLACTIC APPLICATIONS OF PENICILLIN

UNDOUBTEDLY penicillin has proved of value in prophylaxis of infections by susceptible organisms. Intermittent intramuscular injections of aqueous solutions or P.O.B. (suspensions in peanut oil and beeswax) are usually to be preferred. Oral administration, however, may suffice for the prevention of minor infections; likewise, local applications of 5,000 units per gram sulfonamide crystals in postoperative wounds. As a prophylactic measure against infection after surgical or obstetric operations and manipulations, intramuscular injections should be started two or more days before and continued for a variable time thereafter.

Penicillin may be used advantageously in the prevention of (1) infection in traumatic or postoperative wounds and compound fractures; (2) empyema following lung resection; (3) gaseous gangrene following amputations; (4) infection of skin grafts; (5) ocular infections after penetrating injuries, burns, etc.; (6) ophthalmia neonatorum; (7) puerperal infection following abortion or severe dystocia; (8) septicemia following surgical operation or manipulation in osteomyelitis; (9) intracranial infections following operations on the mastoids or sinuses; (10) peritonitis after rupture of the appendix, abdominal wounds, etc.; (11) infection following perforating wounds of the hands or feet; (12) subacute bacterial endocarditis after extractions of teeth, tonsillectomy,

etc.; (13) for the prevention of scarlet fever and streptococcal throat infections in rheumatic carditis, and (14) for the prevention of congenital syphilis by treatment during pregnancy.

THERAPEUTIC APPLICATIONS OF TYROTHRICIN

Tyrothricin is a mixture of gramicidin and tyrocidine produced by *Bacillus brevis*. It is highly active against staphylococci, streptococci, pneumococci, *N. catarrhalis*, *Lactobacillus acidophilus* and mouth spirochetes. It is dispensed as a 2 per cent solution in alcohol and in ointments.

This compound, however, is too hemolytic and otherwise toxic for parenteral administration and is relatively ineffective by oral administration. Consequently it is used only by topical application. A 1:5000 colloidal suspension in *sterile water* (0.2 mg. per cc.) is usually well borne (1 cc. of alcoholic solution in 100 cc. of water).

Tyrothricin is worthy of trial in the prevention and treatment of surface infections by gram-positive organisms including wounds, burns, skin grafts, osteomyelitis, postoperative sinuses, chronic ulcers, sinusitis, mastoiditis, purulent rhinitis, otitis media, empyema, cystitis, suppurative arthritis, ophthalmic infections, furuncles, carbuncles, eczematoid dermatitis, and others.

BACITRACIN

Bacitracin is a new antibiotic agent produced by a member of the *Bacillus subtilis* group.⁹ It has been found highly active against gram-positive organisms, especially streptococci and staphylococci, and its bactericidal activity is stated not to be materially reduced by plasma, blood, pus, and tissue products.

Bacitracin has been employed only in the treatment of local infections by injections of aqueous solutions into lesions (0.1 to 5.0 cc. carrying 100 units), by topical applications of aqueous solutions, or by applications of ointment prepared in a water-soluble base.¹⁰

Its therapeutic value cannot be stated at the present time but it may prove of value in the

otherwise alter treatment as indicated.

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Surgery of the Pancreas

RICHARD B. CATTELL*

LAHEY CLINIC, BOSTON

DISEASES of the pancreas offer many difficulties in diagnosis and, above all, considerable technical difficulties in carrying out curative operative procedures. We have a relatively new field of surgery in the consideration of surgery for pancreatic diseases. For many years there have been sporadic attempts at the elimination of tumors, and many operative procedures for the more common inflammatory diseases involving the pancreas. Except for the catastrophe of acute pancreatitis, the symptoms of pancreatic disease are obscure. Furthermore, we do not have the aids that we have in other surgical diseases, since special studies and special diagnostic aids are of little value in establishing the diagnosis.

The diagnosis of pancreatic disease is usually made by exclusion. In other words, many of the common disorders of the gastrointestinal tract, the kidney, and the retroperitoneal region are first investigated, and when no diagnosis can be established, we then think of this blind area occupied by the pancreas.

Surgical diseases of the pancreas can be divided into three general groups:

1. Those of inflammatory origin. This classification will include the fairly common acute pancreatitis; the less common and little understood chronic pancreatitis—chronic relapsing pancreatitis—which produces marked changes in the gland both structurally and functionally; cysts, many of which are of inflammatory origin; fistulas, either of inflammatory origin or from trauma, and finally calcification or pancreatolithiasis.

2. Congenital disorders, of which little is known. First are included congenital cysts, since congenital fistulas are not encountered. Second, obstruction to the duodenum or to the ducts of the pancreas as a result of developmental failure.

3. Finally, we have a subject which interests us particularly today and has done so during the past twelve years—tumors of the pancreas, which include the benign or hyperfunctioning adenomas and, second, carcinoma.

The symptoms of pancreatic disease are somewhat obscure. These again may be divided into three general groups: (1) those that affect the body mechanism and functions as a whole; general symptoms, which might be weakness, loss of weight, and anemia; (2) those of digestive origin that are chiefly due to interference with the passage of the pancreatic ferments into the intestinal tract, indigestion, anorexia

*Department of Surgery, The Lahey Clinic, Boston, Massachusetts.

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treatment of local infections due to gram-positive organisms resistant to penicillin, like furuncles and other abscesses, carbuncles, infected wounds, ulcers, impetigo, etc.

REFERENCES

1. CALLOMON, F. T., KOLMER, J. A., RULE, A. M., and PAUL, A. J.: Streptomycin and diasone in the treatment of experimental tuberculosis of guinea pigs. *Proc. Soc. Exper. Biol. & Med.* 63:237, 1946.
2. KOLMER, J. A., and RULE, A. M.: Penicillin in the treatment of experimental syphilis of rabbits: II. The synergistic or additive activity of penicillin, oxophenarsine hydrochloride and bismuth and potassium tartrate. *Arch. Dermat. & Syph.* 56:179, 1947.
3. KOLMER, J. A.: The synergistic or additive activity of chemotherapeutic compounds. *Am. J. M. Sc.* (In press.)
4. WEINSTEIN, L.: The spontaneous occurrence of new bacterial infections during the course of treatment with streptomycin or penicillin. *Am. J. M. Sc.* 214:56, 1947.
5. SEELER, A. O., WILCOX, C., and FINLAND, M.: Enhancement of blood levels by caronamide during intramuscular administration of penicillin. *J. Lab. & Clin. Med.* 32:807, 1947.
6. STRAUSS, E., RICHBURG, P. L., SABA, P. Z., and ALEXANDER, J. E.: Enhancement of plasma penicillin concentrations by caronamide and sodium benzoate. *J. Lab. & Clin. Med.* 32:818, 1947.
7. KOLMER, J. A., BONDI, A., WARNER, H. F., and DIETZ, C.: Influence of sodium benzoate by ingestion upon urinary excretion of streptomycin. *Proc. Soc. Exper. Biol. & Med.* 63:455, 1946.
8. KOLMER, J. A., BONDI, A., WARNER, H. F., and DIETZ, C.: Administration of streptomycin in peanut oil and beeswax and in solvecillin. *Science* 104:315, 1946.
9. JOHNSON, A. B., ANKER, H., and MELENEY, F. L.: Bacitracin: a new antibiotic produced by a member of the *B. subtilis* group. *Science* 102:376, 1945.
10. MELENEY, F. L., and JOHNSON, B.: Bacitracin therapy: the first hundred cases of surgical infections treated locally with the antibiotic. *J.A.M.A.* 133:675, 1947.

BETTER DRUG SOUGHT FOR CHILDBIRTH PAINS

TO RELIEVE the pains of childbirth, with safety to mother and child, American chemists have been challenged to produce a new drug better than any now available.

Drug manufacturers were asked to aid in this search by Dr. Bert B. Hershenson of the Boston Lying-In Hospital at the newer analgesics conference of the New York Academy of Sciences.

Specifically, Dr. Hershenson wants a drug that has the advantages without the disadvantages of scopolamine, known to the lay public as the "twilight sleep" producer. This drug, used with apomorphine, is still the best there is for safe pain relief for the woman in labor, Dr. Hershenson and associates believe. Their opinion is based on experiences at their hospital that go back for more than a century.

in order to keep his digestive apparatus working satisfactorily.

The diagnosis of pancreatic cyst will usually be established not by the presence of pain but by symptomless tumor of the upper abdomen. This tumor is localized in the pancreas by the means already outlined, by demonstrating that it is not in the kidneys, spleen, or gastrointestinal tract.

Marsupialization of one of these cysts probably should be done in those cases in which the cyst communicates with the duct system or the duct of Wirsung of the pancreas. Complete excision of the cyst is the best treatment, but it may be necessary to remove the body and tail to accomplish this. This is a difficult technical procedure and I should like to warn against the very close proximity of the inferior mesenteric artery as well as the superior mesenteric artery. It is best to begin the procedure by removing the spleen and lifting up the tail and body of the pancreas from its position in front of the kidney.

A condition in which surgical approach has been tried more recently is that of pancreatolithiasis or calcinosis of the pancreas. The pathogenesis of this disease has but two factors which are known at present. The first is recurrent inflammatory disease of the pancreas; the second factor is the intake of a large amount of alcohol. Nearly all of these patients have an alcoholic history.

These patients have severe pain in the epigastrium, usually passing into the back. These attacks tend to occur with increasing frequency, and may be associated with marked digestive and nutritional disturbances. Nearly all of the patients have a history of morphine addiction, and diabetes mellitus is usually present.

THERE IS very little evidence that can be determined concerning the etiology of acute pancreatitis. Figure 1 is a roentgenogram of a patient who had had repeated bouts of acute pancreatitis and was in a state that might be referred to by Comfort as chronic relapsing pancreatitis. You will see the duct system out-



Figure 1. During routine roentgenographic observation of the upper gastrointestinal tract, regurgitation of barium occurred, outlining the pancreatic duct system.

lined, the duct of Santorini—the accessory duct in the upper portion of the duodenal sweep—and the communicating main duct system or duct of Wirsung, which shows that this is a cause of the patient's symptoms. The problem of handling the situation in these patients is, of course, an extremely difficult matter.

Rarely do we have the benefit of roentgenologic study such as shown in these cases with or without pancreatolithiasis. In Figure 2 we see deformity of the duodenum, a change in the duodenal sweep, in a patient in whom subsequently the diagnosis of chronic relapsing pancreatitis was confirmed.

In Figure 3 an uncommon finding in patients with recurrent pain of pancreatic origin is illustrated. You will see the presence of many calculi scattered throughout the pancreatic head to the right of the lumbar bodies and also continuing through the rest of the gland.



RICHARD B. CATTELL

and bowel changes which may be either constipation or diarrhea, and (3) local symptoms, those that are caused by pressure with the presence or absence of pain.

The diagnostic aids available in attempting to establish a diagnosis of surgical disease of the pancreas first include, of course, roentgenologic studies. These again are part of the exclusion of other causes for the symptoms. In studying the patient, the upper gastrointestinal tract, stomach, and duodenum are fluoroscoped, with particular emphasis on a change in the distance between the first portion of the duodenum and the third, the so-called duodenal angle or sweep; second, elimination of colon disorders; lastly, studies of kidney abnormality.

Since the stool is obviously changed as pancreatic ferments are kept from entering the intestinal tract, we see changes in the character of the stool based on incomplete digestion, on increase in the amount of unbroken protein, the increase in fat, etc.

There are two laboratory tests that may be of value. First is a determination of ferments within the blood stream, particularly the serum amylase; and second, the alkaline phosphatase.

LET us consider some of these disorders, how the diagnosis is made, and how these patients are treated.

Pancreatic cysts are somewhat rare. Their pathogenesis can be on more than one basis. They may originate from acute pancreatitis, as, for example, a case that I should like to present to you briefly. The patient was a young man of 32 who had acute pancreatitis; he was operated on, with drainage of his pancreas in May 1942. In March 1943 a mass developed in the abdomen; for several weeks previously he had had recurrent attacks of epigastric pain. He was again operated on one year after the first operation and a large cyst was found which was marsupialized or attached to the skin so that it would drain to the outside and contract.

This resulted in a pancreatic fistula. In June 1944, approximately another year later, this pancreatic fistula was excised. It remained closed for a period of a few months and again the same type of attacks developed. He was operated on again in an attempt to do a partial pancreatectomy, but because of the inflammation that was present, this was not feasible technically. Finally, because of morphine addiction and recurrence of attacks, another operative procedure was done which was relatively new, although it was done by Fontaine and Leriche some years ago, and has been reported recently by Smithwick and by White.

A thoracolumbar sympathectomy was done to relieve the pain. I should like to call this to your attention as a means of relief of visceral pain in the region of the pancreas, since we have now had a number of cases in which it has been effective. This is an indirect approach to the treatment of pancreatic disease, but it may suffice to enable us to get rid of morphine addiction in these patients.

This man had a bilateral splanchnicectomy from the fifth thoracic through the second lumbar, and since that time he has been markedly benefited as far as relief of pain is concerned. In order to carry him along nutritionally, it is necessary to give him large amounts of pancreatic ferment in the form of pancreatin

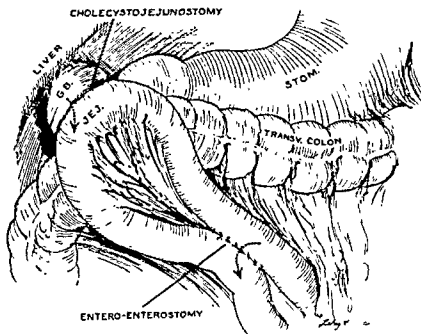


Figure 4. The author recommends this type of first stage operation when two stages are required, antecolic cholecystojejunostomy.

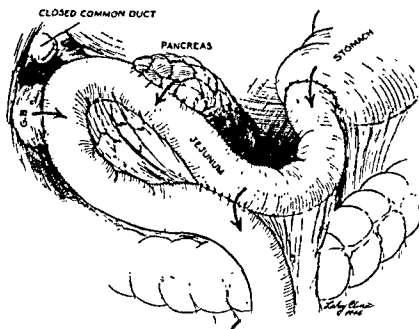


Figure 5. Anastomosis of duct of Wirsung to the jejunum is an essential part of pancreatoduodenal resection. It may be of the open type over a tube, as illustrated, or the closed type, as previously presented by the author.

If most of the pain is rightsided and epigastric, we have been successful in relieving it by sympathectomy on the right side only. In one case, however, in which complete relief of pain was obtained following a right sympathectomy, the patient had pain on his left side after an alcoholic bout and it was necessary to complete the sympathectomy on the other side.

In 1929 the first discrete hyperfunctioning adenoma of the pancreas was reported. Since that time a considerable number has been reported, probably in excess of 250. The first one happened to be malignant. Attention was called to this condition previous to 1929 by Harris, but at the Mayo Clinic, William J. Mayo and his associates reported the first case in 1929.

These patients complain of weakness, fainting attacks, and excessive hunger. They are large consumers of food and frequently awaken at night to take food. This condition may be confused clinically with the petit mal of epilepsy or with carotid sinus syncope. The carotid sinus can be excluded by determining the irritability of the carotid sinus, and the diagnosis can be established only if, during an at-

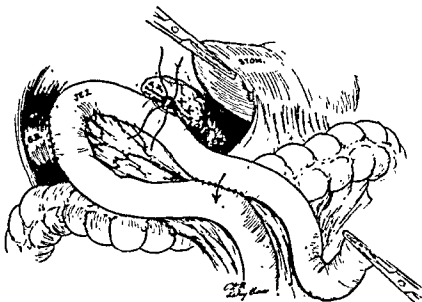


Figure 6. Completed pancreatoduodenal resection, second stage operation, author's method; gastrojejunostomy end-to-end; enteroenterostomy for diversion; pancreatojejunostomy; cholecystojejunostomy, and finally, closure of common duct stump. In the one stage operation the biliary tract anastomosis is choledochojejunostomy.



Figure 2. Deformity of duodenum by an enlarged head of the pancreas due to chronic pancreatitis.

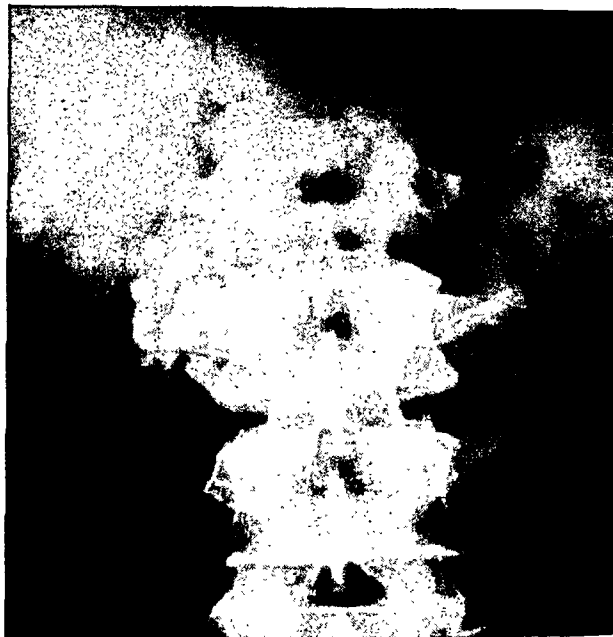


Figure 3. Pancreatolithiasis with stones scattered throughout pancreatic duct system, chiefly concentrated in head. No diffuse calcinosis.

When pancreatolithiasis is present we have a difficult surgical problem to deal with. The best results in this condition, if symptoms are associated with it—they are not always associated with diffuse calcinosis—is a partial pancreatectomy. Particularly if these calculi are scattered through the duct system in the tail and body, partial pancreatectomy will be quite effective.

We have one patient, a woman of 34, who had had recurrent attacks of this type for twelve years. She had lost weight, going from 140 pounds to 110 pounds, and was taking a large quantity of morphine every day. Partial pancreatectomy, including all of the tail, body, and part of the head was accomplished without disengaging the head from the duodenum. In other words, the pancreatic ferments were still left available to the intestinal tract.

After the fifth day following operation she did not have a single dose of morphine nor has she had any difficulty with indigestion, and she has regained her normal weight. Zininger, Whipple, Waugh, and others have car-

ried out more extensive procedures in similar cases in which the pancreatolithiasis or the diffuse calcinosis extended throughout the remainder of the pancreas. This means total pancreatectomy. It is a procedure fraught with great danger. It is questionable whether we are justified in doing a total pancreatectomy for benign diseases, but further experience will prove whether this point is tenable.

It is interesting to observe from the work reported by these men that the amount of insulin required after total pancreatectomy drops unbelievably low. In other words, after total pancreatectomy perhaps 20 or 30 units of insulin daily is all that is required for these patients.

IF ON exploration, partial or total pancreatectomy is not feasible, we must resort to the other procedure of sympathectomy. It is probably unnecessary to go as high as the third or fourth thoracic segment to denervate the region of the pancreas, but that has been done in our cases.

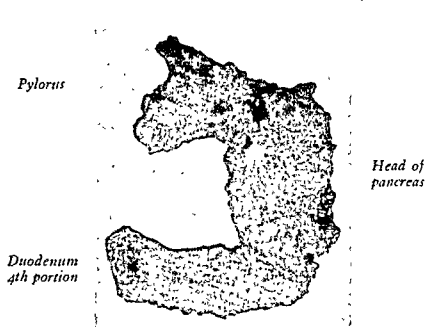


Figure 8. Resected specimen, carcinoma of ampulla, serosal surface. Patient living after five years without symptoms.

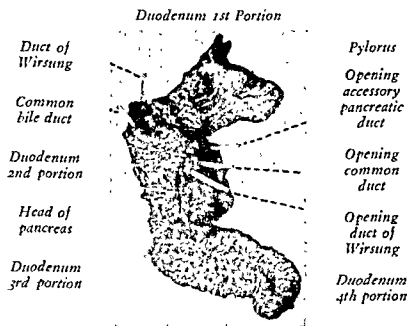


Figure 9. Mucosal surface of specimen in Figure 8, showing submucous invasion of carcinoma of ampulla involving the openings of the accessory pancreatic duct, duct of Wirsung, and common duct.

The condition may be associated with other biliary tract disease, such as stone, in an appreciable number of cases.

This man was operated on and a radical pancreatoduodenectomy was performed.

His immediate postoperative recovery was satisfactory but on his seventh postoperative day a copious amount of clear fluid began to drain from his abdominal wound, indicating a pancreatic fistula. For a period of six weeks this drainage continued as high as 600 cc. of irritating fluid daily.

This man has regained his weight. He has had no recurrence of icterus. The liver has shrunk and he is in excellent condition.

I should like to call attention to some of the important findings in this case for which I am indebted to Dr. Thomas and Dr. Elman.

A deformity of the duodenum was demonstrated. That, in this patient, is important in establishing the diagnosis. This was a carcinoma of the ampulla of Vater invading the duodenal wall. This picture may be produced without obstructive jaundice by duodenal ulcer in the second portion of the duodenum.

A pancreatic fistula developed because the duct of Wirsung was not anastomosed. It is my

opinion and experience after having anastomosed the duct of Wirsung 69 times, that most of the complications of resection for carcinoma of the pancreas are related to failure to put the duct of Wirsung into the intestinal tract. Furthermore, few patients will gain weight properly or handle food properly after operation unless this has been the case.

These patients are poor surgical risks, and everything should be done to improve their status before a radical resection is done. It has been necessary in 50 consecutive resections performed in our clinic to do a two-stage operation in two-thirds of the cases (Figure 4). The easiest first stage is cholecystojejunostomy, which will not interfere with the subsequent resection. An antecolic loop of jejunum is brought up and anastomosed to the full width of the gallbladder. Even if you do not choose to do the resection, if you think it is a favorable case you will be doing your best by this patient if this operation is carried out (Figure 4), and give him the chance of possible subsequent resection without too much technical difficulty.

Figure 5 shows the anastomosis to the duct of Wirsung. It is not a difficult procedure. As I have said, we now have done this in 69 cases.



Figure 7. Postoperative roentgenographic visualization of the upper gastrointestinal tract twelve days after one stage pancreaticoduodenal resection.

tack, the blood sugar level is 40 mg. per 100 cc. or below.

The treatment of this condition is obviously excision of the adenoma. Our experience is confined to 9 cases which have been reported by my associates, Drs. Marshall and Allan. It is extremely difficult to locate these small tumors within the pancreas. It is done by division of the gastrocolic omentum, dropping the colon downward, and then searching the entire surface of the pancreas. If the adenoma is not discovered (it may be only a few millimeters in diameter) the pancreas must be freed up and further search made. If this study is unsuccessful, it will be necessary to do partial pancreatectomy.

IMPORTANT advances in surgery of the pancreas have followed the report by Whipple and his associates in 1935 of their work on suc-

cessful radical removal of carcinoma of the head of the pancreas.

Obviously, if anything is to be accomplished in cancer of the pancreas it can be done only by resection. In a group of 56 consecutive patients operated on before 1935 with the best palliative type of procedure performed—cholecystojejunostomy—75 per cent were dead within six months of their operation or within nine months of their first symptoms. This is a standard to which the comparison of results of resection can be made.

The patient on the platform is a man 67 years of age who was admitted to the hospital in St. Louis on the service of Dr. Elman and Dr. Thomas in May 1947. This man had had symptoms for six months. I would like to call your attention to the importance of bowel symptoms as a possible indication of pancreatic disorder. He had had no passage of blood, but had noticed increasing constipation. Subsequent to this he began to lose his appetite and then had complete distaste for food. He lost 50 pounds in six months, dropping in weight from 190 to 140 pounds. This was partly due to reduced food intake.

Icterus, pruritus, dark-colored urine, and clay-colored stools developed. When the patient was admitted to the hospital the icterus index was in the neighborhood of 45. While the patient was being studied medically, the icterus index rose after a few days' interval to 65, and previous to the time of his operation, which was done around June 10, 1947, it reached 90.

The liver was enlarged down 4 fingerbreadths below the costal margin. It is essential in establishing a diagnosis of cancer of the pancreas that the liver is enlarged in the presence of obstructive jaundice. Whether one feels the gallbladder or not, the liver must be enlarged. Sometimes the gallbladder is pushed so far laterally by enlargement of the liver that it cannot be felt, but usually with care one can feel a rounded mass projecting below the firm, sharp edge of the liver. This is necessary to establish the diagnosis of malignant disease in a patient with obstructive jaundice. It is usually, but not necessarily, painless.

The Diagnosis and Treatment of Hydronephrosis

HERMAN L. KRETSCHMER*

UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE, CHICAGO

THE PATIENT we will discuss here is 58 years of age. She came to the outpatient department at Barnes Hospital on February 21, 1947, and I am indebted to that department for the privilege of presenting her to you.

Two months before she came to the clinic, she noticed a mass in her abdomen. In September 1946, she developed attacks of nausea and vomiting. These attacks occurred every week or two. Following these attacks, she lost weight, tired easily, and had a dull ache in her flank. She also complained of frequency of urination, both day and night, so that she was obliged to void every two hours.

On physical examination the abdomen was rather prominent. A mass about the size of a large grapefruit was felt in the left upper quadrant. This mass was markedly tender, freely movable, and slightly irregular. No stone shadows were seen on roentgenologic examination.

An intravenous urogram showed the presence of a large hydronephrosis on the left side. There was no visualization of the dye on the right side.

*Professor of Urology (Rush), University of Illinois College of Medicine; President of the Interstate Postgraduate Medical Association of North America, 1948.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

Cystoscopic examination revealed the presence of marked trabeculations and some bladder diverticula. The right ureteral orifice could not be found on the first or subsequent cystoscopic examinations. The left ureteral orifice appeared normal.

This patient was operated on and a plastic operation at the ureteropelvic junction was carried out.

DR. KRETSCHMER: Madam, how do you feel?

PATIENT: Fine.

Examination shows the presence of a scar. The most recent intravenous urogram still shows the presence of some hydronephrosis. When this urogram is compared with the film which was made before the operation, a great diminution in the size of the hydronephrosis is evident. This lady has had a wonderful result and I believe there will be still further improvement in her case. She states that she feels very well and is stronger than before her operation.

She mentioned a very interesting symptom; namely, that when she washes on the washboard and bends over it, she has pain in her flank. I believe this is due to the fact that the hydronephrosis does not completely empty. The reflex nausea and vomiting have disappeared. The frequency of urination is still present and is probably caused by the persistence

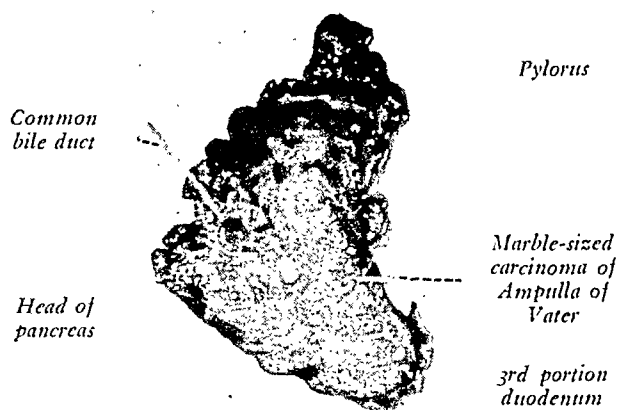


Figure 10. Resected specimen, serosal surface; patient living after four and one-half years.

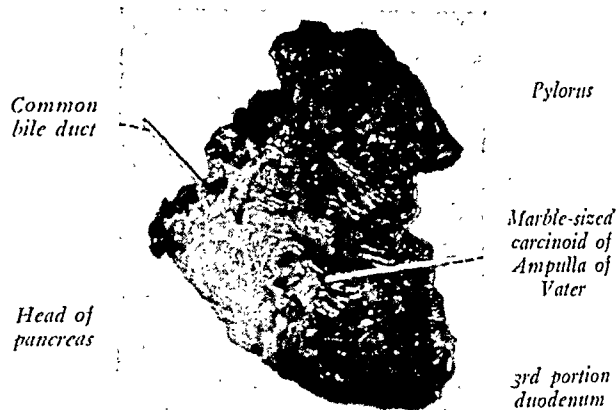


Figure 11. Mucosal surface of specimen in Figure 10, showing ulcerated carcinoid of ampulla of Vater.

You will see in the upper part of the illustration that a tube has been implanted in the duct of Wirsung and an end-to-side anastomosis has been done.

In Figure 6 is shown the completed operative procedure and the technic as worked out by us in our clinic. You will see an antecolic end-to-end gastrojejunostomy, then an enteroenterostomy, then a pancreatojejunostomy, and finally, a choledochojejunostomy or cholecystojejunostomy, depending on whether it is a one-stage or two-stage procedure.

Figure 7 shows the status twelve days after operation. No pancreatic fistula had developed because of the anastomosis of the duct.

I should like to show you the specimens taken from 2 patients. Most of us have the idea that if cancer of the pancreas is present, little can be accomplished. In 50 patients on whom we have operated there have been 9 operative deaths, a mortality rate of 18 per cent. A patient who was operated on five years and two months ago, is at present normal in every respect; she has had no symptoms since her operation over five years ago (Figure 8).

Figure 9 shows an ulcerating tumor of the ampulla in this same patient which had spread

to involve the entrance of the common bile duct, the entrance to the duct of Wirsung, and also the accessory pancreatic duct or duct of Santorini. One gland along the border of the duodenum was involved but the patient still remains well.

The next patient is a man of 64 who was operated on (Figure 10) a little over four years ago. He has continued to be well after radical pancreatoduodenal resection. Figure 11 shows this ulcerating tumor with metastases to regional lymph nodes; this proved to be a carcinoid of the ampulla of Vater.

It is our opinion that an operative procedure has been developed through the efforts of many surgeons which not only gives us a reasonable opportunity to eliminate and remove carcinoma of the pancreas with great immediate improvement, with a minimum, perhaps, of complications, but furthermore, over a period of some years the mortality has been gradually reduced. In a group of 50 patients who have had this operation, in our experience, the rate so far during a period of observation of from one to five years has been approximately 40 per cent survival without the appearance of any evidence of recurrence.

TABLE 1

UROLOGIC CAUSES OF HYDRONEPHROSIS

KIDNEY	BLADDER
CONGENITAL ANOMALIES	ANOMALIES
Form	Ectopia
Size	Diverticulum
Number	Other anomalies
Position	TUMORS
Vascularization	Carcinoma in region of ureteral orifice
LESIONS OF PELVIS	Papilloma in region of ureteral orifice
Stone	Extensive carcinoma
Tumor	HYPERTROPHY OF INTERNAL URETERAL RIDGE
Blood clots (cause?)	URETHROVESICAL
URETEROPELVIC JUNCTION	LESIONS OF PROSTATE
Stone	Chronic prostatitis
Stricture	Benign prostatic hypertrophy
Aberrant artery	Carcinoma
Periureteral adhesions	Bars and contractures
Narrowing at ureteropelvic junction	Cysts
URETER	Posterior valves
Stone	Hypertrophy of verumontanum
Stricture	URETHRAL LESIONS
Tumor	STRICTURE
Blood clots	Congenital
Periureteral adhesions	Acquired
Compression by tumor	PHIMOSIS
Cystic dilatation at vesical end	OTHER RARE LESIONS
Valves	Stone
Atony	Tumor
Anomalous insertion	Diverticulum
	Urethrocele

TABLE 2

EXTRAURINARY CAUSES OF HYDRONEPHROSIS

PREGNANCY	GASTROINTESTINAL
GYNECOLOGIC LESIONS	RECTUM
UTERUS	Carcinoma
Carcinoma	COLON
Fibroid	Carcinoma
Endometriosis	RETROPERITONEAL
OVARY	Tumors
INTRALIGAMENT (CYSTS AND TUMORS)	CENTRAL NERVOUS SYSTEM
VAGINAL CARCINOMA	Tabes
	Myelitis
	Spinal cord tumors
	Compression fracture

a stone, a stricture, an aberrant artery, or periureteral adhesions.

The management of the patient with periureteral adhesions is relatively simple. One divides and removes the bands of adhesions. In some patients it may be necessary to do a nephropexy. In the patient with an aberrant artery, the question of whether the aberrant artery causes the hydronephrosis or whether the hydronephrosis began independently of the aberrant artery arises. When the aberrant artery is small, i.e., when it supplies a small segment of kidney, the artery may be divided. On the other hand, if the artery is large and supplies a large segment of the kidney, it may be necessary to transplant the ureter to avoid obstruction by the aberrant artery.

The patient with a stone at the upper junction calls for a pyelotomy and removal of the stone. The patient with a stricture must be operated on. The number of operations that have been recommended for management of this condition are legion, and I shall not discuss the various advantages claimed for the operations devised by the different authors. Recently Davis of Philadelphia recommended a simple procedure of dividing the stricture and splinting the ureter with a small, soft rubber catheter. It is hoped that this simple procedure will accomplish the desired results, since it is technically much easier and simpler to perform than the various types of plastic operations.

for hydronephrosis are varied. It is a relatively common urologic condition. As I have mentioned, it may exist as a silent condition and may never produce symptoms referable to it. In some cases, however, the symptoms are atypical, and the most important problem is the determination of the underlying cause. The causes of hydronephrosis may be urologic or extraurinary in origin, as shown in Tables 1 and 2.

From a review of the multiplicity of causes, it is obvious that there is no specific treatment for the hydronephrosis, but that treatment must be directed towards removing the cause. In a case of hydronephrosis, such as the patient I have discussed, it is obvious that she has an obstruction at the ureteropelvic junction. The obstruction generally is due to the presence of



HERMAN L. KRETSCHMER

of a urinary infection due to *Bacillus pyocyaneus*.

From the history and physical examination, it was evident that the mass in the left upper quadrant was renal in origin. An intravenous urogram showed the presence of a large hydronephrosis on the left side. Because there was no visualization of the dye on the right side, repeated cystoscopic examinations were made to determine the status of the right kidney. They failed to reveal the presence of a ureter on the right side. This patient has but one kidney and this kidney is the seat of hydronephrotic change. The diagnosis, therefore, was obvious: hydronephrosis in a solitary kidney.

I SHOULD like to dwell on the interesting fact that the cystoscopic examination showed the presence of diverticula. Diverticula, it is now believed, are always congenital in origin and due to obstruction at or in front of the neck of the bladder. They are rarely observed

in women; thus, the presence of diverticula should at once cause us to suspect that this patient has an obstruction at the neck of the bladder. Therefore, in addition to management of the hydronephrosis, our attention must be directed to her bladder.

Since her operation, this patient has had an uneventful convalescence. It can be seen by comparing the pyelograms that were made that the hydronephrosis is smaller, the pain is less, and the nausea and vomiting have disappeared. A recent examination showed that the elevated nonprotein nitrogen level has returned to normal (33 mgm. per cent). On the other hand, she still has some urinary infection as evidenced by the pus and bacteria in the urine, and some frequency of urination.

The urinary infection did not improve following treatment with penicillin, sulfadiazine, and sodium acid phosphate. It is evident, therefore, that she has some infection either in her bladder due to obstruction at the bladder neck, or residual infection in her kidney pelvis. If she does not have residual urine, it might be well to catheterize her ureter and obtain urine for bacteriologic studies. In view of the fact that antibiotics have not been of much help, it might be well to dilate her ureter or at least irrigate her kidney pelvis with silver nitrate (2 per cent).

The symptoms of hydronephrosis are not always typical. You are all familiar with the fact that in some patients hydronephrosis may result in complete atrophy of the kidney and there are no symptoms referable to the urinary tract. In a certain group of patients, hydronephrosis is discovered in a more or less routine manner. Many such patients with hydronephrosis consult the internist because of some stomach or intestinal disturbances and routine intravenous pyelograms reveal the cause of gastrointestinal symptoms to be due to hydronephrosis.

Let us now consider the subject of hydronephrosis in its broadest aspects. The most important problem in any case of hydronephrosis is the determination of the underlying pathology. It is to be remembered that the causes

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DIAGNOSTIC CLINIC

The Farmer's Back

ROBERT D. SCHROCK*

UNIVERSITY OF NEBRASKA, OMAHA

IN OUR midwestern section of the United States, the problem of "the farmer's back" has been far more disturbing and more frequently encountered during the past ten years than in any previous period in our experience.

"The back in industry" has received many pages of attention in medical literature. Farmers are in the essential industry of food production. As self-employers, they are not influenced by disability covered by compensation insurance. Farmers, as a rule, are eager producers and possess a "will to work" and a "will to get well." These attributes are valuable aids to effective therapy.

The relative increased incidence of back disabilities in farmers is, in our opinion, explainable by the following causes: (1) chronic fatigue due to long hours of work and lack of adequate help; (2) minor trauma, frequent and prolonged, from machinery that is twisting and vibratory in type; (3) decreased muscle strength as a result of motorization of farm equipment; (4) education by the press and medical profession, and (5) improved financial status.

*Professor of Orthopedic Surgery, University of Nebraska, Omaha.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

At the Cleveland meeting in 1946, the problem of "low back pain" was presented from the standpoint of examination and diagnosis. This presentation will emphasize more definitely the therapy in the various conditions.

EPIPHYSITIS VERTEBRALIS JUVENILIS

The incidence of this condition in farm boys and girls has decreased. Life on the farm for growing children is less arduous than in the previous decade. The viewpoint of farm parents is less adamant than in days gone by; there has developed a greater respect for the human "growing critter"; thus, greater protection against undue physical strain has resulted. These altered and more intelligent viewpoints are readily traceable to the activities of the 4-H Clubs which so broadly cover this great central farm area. These clubs teach the modern concepts of nutrition and health.

The severe dorsal rounding which was seen not infrequently twenty-five years ago is now, in our experience, a rarity. The family and family doctor have been major factors in effecting the disappearance of this clinical entity. At present, when these youngsters complain of high back pain, they receive early attention before deformity occurs. With adequate nutrition, minor medication, and light external sup-



Figure 1. Epiphysitis dorsalis vertebrae, mild degree.



Dr. Schrock with a patient, showing epiphysitis of vertebrae, in low dorsal region, involving upper lumbar as well, with marked deformity, loss of normal dorso-lumbar contour, definite increase in lumbar lordosis.

port, symptoms disappear within six months, and bone growth in the vertebral epiphyses is within normal limits in one year.

During the past ten years an effort has been made to accuse a misbehaving thyroid gland of being contributory to these disorders of growth. Investigations, to date, do not show complete agreement in their conclusions. It is agreed that an adequate milk intake, with consistent use of cod liver oil or its derivatives, is good medicine. Indiscriminate use of thyroid extract in these children and laxity in continuous clinical observation may lead to untoward dangerous effects.

ACUTE TRAUMATIC MYOSITIS

Acute myositis, traumatic in origin, usually results from sudden strain in unanticipated adverse positions, or from injudicious effort during a state of exasperation. The muscle or aponeuritic injury is frequently to the sacrospinalis. Early muscle spasm results as a protective physiologic mechanism. This painful spasm prevents further damaging activity. Normal repair processes, when undisturbed, require

two to three weeks. Adjuvants to recovery are rest, local heat of moderate degree, and relaxing massage. The use of "pain killers" and local anesthetics is still a debatable procedure except from the standpoint of quick and temporary relief. There is an increasing tendency toward "trigger point" injections for many acute sprains. The procedure may be desirable under certain conditions but widespread use is, in our opinion, not to be recommended.

ACUTE INFECTIOUS MYOSITIS

The symptomatic diagnosis of "lumbago" is more understandable to the patient than is the etiologic diagnosis of acute infectious myositis. The history may show recurring attacks of "lumbago" with increasing frequency. These attacks are precipitated by undue lifting strain, exposure of an overheated back to quick cooling, or sleeping in a draft, or may result subsequent to a minor sore throat, toothache, blocked sinus, or short period of constipation. These re-

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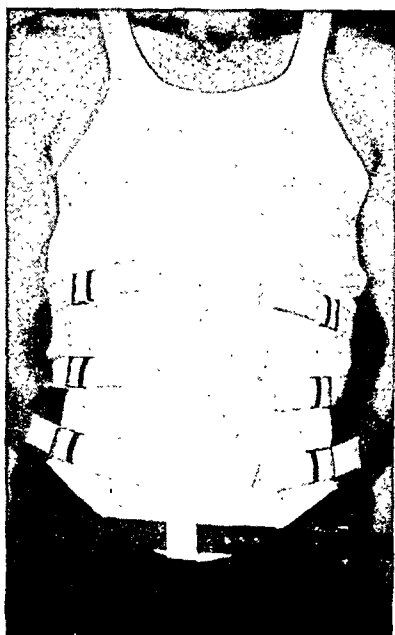
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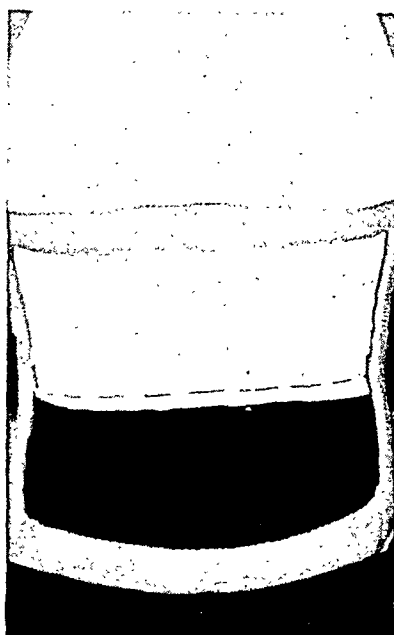
Arthritis transverse process LV articulating on S1—Resection.



Arthritis spine—fusion in good position.



Skeleton brace with Taylor bars.



Skeleton back brace—back.



Skeleton back brace—front.

current attacks of "lumbago" are precursors or prodromals of the chronic fibrositis of middle age, and the osteoarthritis of later years.

Prophylactic treatment is directed toward meticulous search for foci of infection and judicious removal of the demonstrable foci. Multiple foci may show infections of differing types, but with synergistic effects upon muscle or joint. The major effect may be sufficient to maintain the patient's general health at a low level, and so offer less resistance to the toxic effects of absorption. Warm clothing, with slow cooling after exertion, prevents sudden changes in capillary circulation and materially aids in removal of fatigue products from the heavy musculature of the back. Few middle-aged backs will withstand the rigor of cold showers.

The definitive care is directed toward relief of muscle spasm through local heat of gratifying dosage, massage to stimulate circulation, and salicylates to the saturation point. Active stretching, with motion limited to the pre-pain point, is of value. Overactivity and overstretching will only prolong the attack.

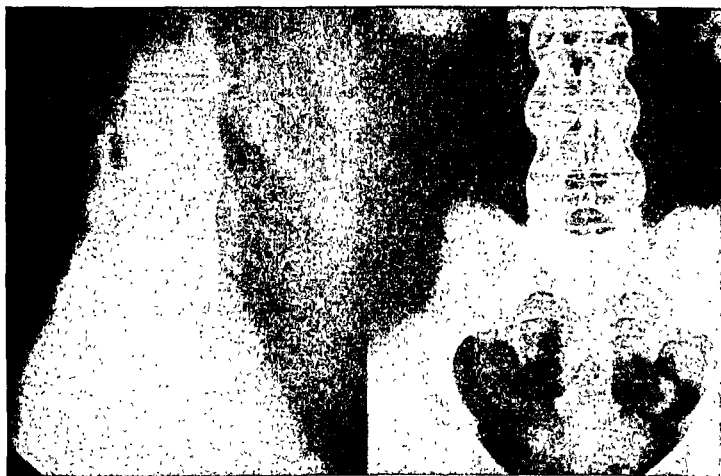
CHRONIC MYOSITIS, MYOFASCIITIS, AND FIBROSITIS

THE clinical "stiff back," presenting some limitation of motion, generalized increased muscle firmness, lack of elasticity, and diffuse tenderness, is given a variety of names. The lack of definitive terminology is evidence of our present concept of the basic condition. There is a comparable lack of uniform agreement as to its etiology, and not too definite an idea of the over-all pathology. The motor mechanism of the back is complicated. Muscles, as a result of repeated trauma, low grade infection, and disuse with resulting poor blood supply, may undergo degenerative changes chiefly showing as fibrous tissue. This leads to structural shortening of muscle, muscle sheaths, and aponeurotic attachments.

Gliding motion in the intermuscular planes is essential for free mobility. Hemorrhage or exudate within the fascial spaces, if not promptly absorbed, becomes organized tissue with localized fibrous adhesions or complete obliteration of the intermuscular gliding mechanism.



Arthritis transverse process LV articulating on S1—Resection.



Arthritis spine—fusion in good position.

The spinal ligaments gradually lose their elastic tissue elements, and the back presents the board-like aspects of an advanced degree of fibrosis of all soft part structures.

THERAPY in the advanced case is prolonged, arduous for patient and doctor, and too often discouraging for all concerned. Elimination of the so-called "rheumatoid" elements is essential for ultimate success. Any and all physical therapy measures for promotion of local circulation are valuable. The most valuable agent is active exercise by the patient, guarded stretching, and back mobilizing efforts without overactivity.

The method of determining the most beneficial dose of activity is one of trial and error. It is in this type of back disability, when "trigger point" tenderness is presented, that injection of local anesthetics proves most satisfactory. Manipulation of the fibrositic back, under general anesthesia, is not as yet an established procedure. A supporting apparatus, intermittently used, will permit these patients to be partially productive.

OSTEOARTHRITIS OF SPINE

This condition prevails in the age group of "50 years and more." The onset is insidious, may be even symptom-free, or follow the pattern of an infectious myositis. The productive process may be well advanced before it is even recognized.

For complete information of the causes and treatment of arthritis of all types, one needs only to scrutinize an editorial in the J.A.M.A., October 3, 1947. The frank confession of failure is commendable. The honest recognition of certain useless therapeutic methods is highly laudable. The editorial pulls no punches, and demonstrates a high degree of courage.

The usual reason for pain in osteoarthritis of the spine is trauma superimposed on an already established and irreversible pathologic change. Recovery from the trauma is prolonged and hence, help is sought. Our help is limited to careful analysis of activities that pro-

duce trouble, and to urging their avoidance. Adaptation of the back to its capacity is essential. Maintenance of the general health of the patient at a high level, and the use of a supporting back brace are helpful.

SPONDYLOLYSIS—SPONDYLOLISTHESIS

In this category, patients present a lumbar vertebra, practically always the fifth, in which the laminae of the neural arch are connected to the posterolateral aspects of the vertebral body with fibrous tissue rather than with bone. This defect adds to the architectural weakness, and diminishes resistance to mechanical strain. Due to the anterior inclination of the sacrum and the normal anterior lumbar curve, there is at the lumbosacral junction a shearing force that tends to thrust the fifth lumbar forward on the sacrum. This gliding forward action is gradual, and may take place in varying degrees without symptoms of real pain. These patients, under conditions normal to them, have "backaches" made worse by overuse or repeated heavy lifting. Severe twisting or lifting strains may produce minor backache but sudden forward shifts are accompanied by severe pain and persisting low back disability. Frequently there will be associated nerve root pressure or stretch, giving rise to lateralized or radiating pain over the distribution of the fifth lumbar or first sacral nerve, unilaterally or bilaterally.

The literature on this condition is extensive. There is still no uniformity of opinion in classifying this condition as a congenital anomaly, or as a trauma at birth, produced by certain maneuvers in making the newborn breathe. Rarely is the condition diagnosed early in life, for displacement, if present, is minimal. It proceeds gradually and slowly. Some adolescents may complain and refrain from exposing their backs to the strains normal for such ages. Many adults recognize their possession of a "weak back" and yet continue with heavy work until pain becomes disabling. This occurs most frequently after the age of 35, when muscle tone, strength, durability, and quick recovery from fatigue tend to decrease.

In this middle and older age group, acute

trauma and chronic overfatigue produce disability greater than anticipated and recovery from a "sore back" does not take place.

When spondylolysis is discovered in childhood or adolescence, conservative care (sufficiently informative) and prophylactic observation may be adequate. In late adolescence and in adult life, external bracing is essential until internal bracing can be accomplished by means of a low back fusion.

There is a general consensus, supported by many clinical observations, that forward displacement of the fifth lumbar takes place gradually; that correction of the displacement is impossible in grades 3 or 4 and improbable in grades 1 and 2; that operative fusion is most desirable and more successful when displacement is minimal.

CONGENITAL MALFORMATIONS

Detailed studies of patients with low back pain reveal a high incidence of architectural abnormalities in the spine. Osseous variations



Spondylolisthesis, Grade III.



Spondylolisthesis, Grade I—Low back fusion.

The spinal ligaments gradually lose their elastic tissue elements, and the back presents the board-like aspects of an advanced degree of fibrosis of all soft part structures.

THERAPY in the advanced case is prolonged, arduous for patient and doctor, and too often discouraging for all concerned. Elimination of the so-called "rheumatoid" elements is essential for ultimate success. Any and all physical therapy measures for promotion of local circulation are valuable. The most valuable agent is active exercise by the patient, guarded stretching, and back mobilizing efforts without overactivity.

The method of determining the most beneficial dose of activity is one of trial and error. It is in this type of back disability, when "trigger point" tenderness is presented, that injection of local anesthetics proves most satisfactory. Manipulation of the fibrositic back, under general anesthesia, is not as yet an established procedure. A supporting apparatus, intermittently used, will permit these patients to be partially productive.

OSTEOARTHRITIS OF SPINE

This condition prevails in the age group of "50 years and more." The onset is insidious, may be even symptom-free, or follow the pattern of an infectious myositis. The productive process may be well advanced before it is even recognized.

For complete information of the causes and treatment of arthritis of all types, one needs only to scrutinize an editorial in the J.A.M.A., October 3, 1947. The frank confession of failure is commendable. The honest recognition of certain useless therapeutic methods is highly laudable. The editorial pulls no punches, and demonstrates a high degree of courage.

The usual reason for pain in osteoarthritis of the spine is trauma superimposed on an already established and irreversible pathologic change. Recovery from the trauma is prolonged and hence, help is sought. Our help is limited to careful analysis of activities that pro-

duce trouble, and to urging their avoidance. Adaptation of the back to its capacity is essential. Maintenance of the general health of the patient at a high level, and the use of a supporting back brace are helpful.

SPONDYLOLYSIS—SPONDYLOLISTHESIS

In this category, patients present a lumbar vertebra, practically always the fifth, in which the laminae of the neural arch are connected to the posterolateral aspects of the vertebral body with fibrous tissue rather than with bone. This defect adds to the architectural weakness, and diminishes resistance to mechanical strain. Due to the anterior inclination of the sacrum and the normal anterior lumbar curve, there is at the lumbosacral junction a shearing force that tends to thrust the fifth lumbar forward on the sacrum. This gliding forward action is gradual, and may take place in varying degrees without symptoms of real pain. These patients, under conditions normal to them, have "back-aches" made worse by overuse or repeated heavy lifting. Severe twisting or lifting strains may produce minor backache but sudden forward shifts are accompanied by severe pain and persisting low back disability. Frequently there will be associated nerve root pressure or stretch, giving rise to lateralized or radiating pain over the distribution of the fifth lumbar or first sacral nerve, unilaterally or bilaterally.

The literature on this condition is extensive. There is still no uniformity of opinion in classifying this condition as a congenital anomaly, or as a trauma at birth, produced by certain maneuvers in making the newborn breathe. Rarely is the condition diagnosed early in life, for displacement, if present, is minimal. It proceeds gradually and slowly. Some adolescents may complain and refrain from exposing their backs to the strains normal for such ages. Many adults recognize their possession of a "weak back" and yet continue with heavy work until pain becomes disabling. This occurs most frequently after the age of 35, when muscle tone, strength, durability, and quick recovery from fatigue tend to decrease.

In this middle and older age group, acute

trauma and chronic overfatigue produce disability greater than anticipated and recovery from a "sore back" does not take place.

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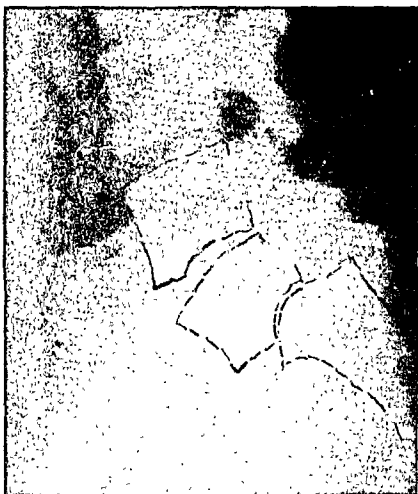
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LOW BACK INJURY WITH PAIN IN THE LOWER EXTREMITIES

are most frequent in the lumbosacral region, which is admittedly the recipient of most back strain. Back strength is determined by its weakest region. Abnormal architecture indicates structural weakness which many times lacks adequate muscle strength to compensate for bone defects. Low back decompensation is more frequent in the presence of congenital malformations of the lumbosacral region.

This statement does not mean that all backs showing congenital malformations cause trouble for their possessors. Fortunately, many backs do not have to withstand the wear and tear of farm life.

When low back decompensation does occur, it is sometimes possible for the farmer to plan his work in such a way that he can avoid those recognized strains. The intelligent farmer will use his head and the other fellow's back. Back efficiency and symptomatic relief is obtained with a light nonrigid low back support, to be used as the occasion demands. Conservative care is indicated until proved a failure. The trial period is usually three to six months. When conservative measures fail, low back fusion is indicated.

During the past ten years, the problem of herniation of the nucleus pulposus, with associated compression neuritis, has properly received major attention. The enthusiasts who early proclaimed this lesion as the causative factor in all low back pain with sciatica, have gradually had their enthusiasm tempered by more adequate follow-up studies of their generous and brilliant laminectomies. The early use of contrast opaque media injected into the spinal canal is not employed as freely, as closer clinical study is finding methods for more adequate localization of the lesion.

Laminectomies are becoming less generous, and technic has improved. More adequate follow-up studies are demonstrating that resection of the herniated nucleus pulposus in many cases does not give adequate satisfaction to the patient or doctor. There is developing a strong sentiment that low back fusion should be done with all laminectomies. This viewpoint is too radical. However, a combination of congenital malformation and signs of localized nerve root pressure is now being more generally accepted as an indication for low back fusion.



Hemi-vertebra, Lumbar V.



Hemi-vertebra, Lumbar V—Low back fusion.

Differential Diagnosis, Benign Prostatic Hypertrophy, and Neurogenic Bladders

DALTON K. ROSE*

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

PROSTATIC hypertrophy (requiring surgery) occurs in probably 35 per cent of men past the age of 60. Presented in another way, it occurs in about 67 per cent of all men, with about half of all these cases eventually coming to surgery.

A point of interest is that the term hypertrophy of the prostate makes us feel that the gland has to be large to obstruct the bladder. However, obstructing factors, scar tissue, or a small adenoma which may be buttressed against scar tissue down in the prostatic urethra, will obstruct equally. In other words, you can have a giant prostate with no obstruction and you can have a 2 gm. prostate with considerable obstruction associated with contracture at the vesical neck.

The contracture type occurs in younger men and is associated with infection in all instances. In that respect it is going to be interesting to see what sulfonamides and the new antibiotics do in the next generation to scar type obstruction, whose frequency of occurrence should be reduced.

The adenomatous type is due to senescence,

*Professor of Clinical Genitourinary Surgery, Washington University School of Medicine, St. Louis.

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of course, and goes hand in hand with graying hair, bald head, wrinkled skin, etc. Although all men have some scar or hypertrophic changes, only a small percentage of them come to surgery.

The trick of prostatic obstruction is, in my opinion, how rapidly it develops. If one is required to lift an impossible load but is given time enough to develop the necessary strength to lift the load, it may become possible. Although the bladder is smooth muscle, if it is given time when obstructed, it will develop a thick muscle wall back of the obstruction. The obstruction may stop anywhere in life and one may develop sufficient compensation or thickening of the bladder wall to overcome the degree of obstruction. Such a man will notice in particular that he urinates in the morning with a slow stream, due to overfilling of the bladder during sleep and a slight overstretching of the bladder wall, which though compensated now when overstretched, does not force the stream out as easily as it does later in the day when the bladder is emptied more frequently.

Stimulation to the bladder is nothing more nor less than stretch. The stretch reflex, of course, is in smooth muscle just as in striated muscle. The "knee jerk" is stretch reflex. A bladder filled and emptied is in effect a stretch re-

flex. On rising in the morning, a few drops dribble out, then a little more and a little more, and finally a stream when the bladder wall is contracted to a sufficient point that it has strength to overcome the obstruction.

Nycturia is explained in this way: When a man goes to sleep, inhibition by the brain is relatively lost and the thickening bladder wall goes into uncontrolled contraction. This contraction wakes him with a desire to void. He may get up and void or he may roll around in bed in discomfort, but when he finally does get up, he may find that he does not have to void as badly as he did when he was in bed; he is awake, his inhibition is back, and his bladder wall has gone out of contraction. On the other hand, when he carries a residual urine, he may have less nycturia due to a developing pressure anesthesia to his bladder. This occurs in the same manner as when you sit on your hand or lie on your arm. It is a pressure numbness that comes to the bladder when there is either a very high intracystic pressure or a residue of urine in the bladder all the time.

Frequently when a patient comes to you with 1000 cc. of residual urine he has no distressing desire to void. You can remove the 1000 cc. and you will not be able to get back more than 500 or 600 cc. In that split second, so to speak, the pressure anesthesia has partially disappeared even in a bladder wall which became overstrong for a long period before it finally gave way.

ALL of this brings us to the point that prostatic obstruction is not alone the prostatic obstruction; it is in a large part decompensation of the bladder wall. You can prove this just by realizing that if you could always raise intracystic pressure you would never have complete obstruction, although it might come to the point where the stream would be 10 feet long and as large as a darning needle.

To go into an analysis of neurogenic bladder—a misnomer, in my opinion, as the term suggests that the nerves of the bladder are pri-



DALTON K. ROSE

marily at fault—I do not think it is the bladder itself that is neurogenic, but rather I think the primary nerve damage is to the so-called voluntary sphincter. We have detrusor action but there is no detrusor muscle unless one wants to consider it as the bladder wall. We have already covered the fact that normally the bladder wall changes according to the load that is offered it; if it becomes thick, and if the block is such that the back pressure continues indefinitely, it becomes overstretched and has no expulsive power. There are many gradations between, which you can readily realize, and all these gradations give characteristic symptoms of either frequency in the early day, with a thickening bladder wall, or, paradoxically, incontinence at the time when it overflows, when the bladder is stretched thin and always full but always running over.

I have reported previously a standard for normal bladder function. I do not believe these standards can be proved until we have satisfactory x-ray motion pictures. However, these

ideas of bladder physiology stand the scrutiny of all investigative work up to this time and also the scrutiny for analysis of all types of bladder symptoms. The main idea is that the bladder is a voluntary-involuntary organ. It is not at all unlike swallowing. You chew voluntarily to a certain degree, swallow, the food goes down to the involuntary portion of the swallowing apparatus, where it gets away from you and away it goes; you cannot recall it. The first part is voluntary and the last part is involuntary, and so it is with urination. If the bladder were not locked, so to speak, by voluntary control, there would be no time or place for emptying the bladder; it would run all the time or spasmodically.

What is the voluntary action? It is the anterior perineal muscles. You can see a great deal of this action in cystoceles, rectoceles, and urethroceles. It is the perineal muscles anterior to the anus, although the entire pelvic sling has something to do with it. These muscles are, of course, striated, voluntary, and innervated by the pudic nerve, which is of sacral origin and is thus related to the sciatic nerve, which is lumbosacral in origin. But that is not of great importance except in physiologically differentiating certain types of neurogenic bladders, in which the anal sphincter, voluntary bladder sphincter, and the legs exhibit similar nerve changes from spastic to atonic. I wish to differentiate uncomplicated types of neurogenic bladders that you can diagnose by feeling the anal sphincter only, without any other method.

If the perineum is the voluntary control of a voluntary-involuntary sphincter complex, what are the steps in urinating? The first step is to choose the time and place. The next is to lower the anterior perineum, which brings down the internal orifice of the bladder. A thin muscle called the trigonal muscle bridges the internal orifice of the bladder; when the perineum pulls down the internal orifice of the bladder, this muscle, going through and over the floor of the internal bladder orifice, is lowered, contracts, and so lowers and broadens the internal orifice. Herewith ends the voluntary phase of urination. Urine now runs over into the

posterior urethra to stimulate involuntary bladder contraction. Control, therefore, can voluntarily be exerted by pulling up on the perineum. You have seen children run crosslegged. Why do they do this to keep from urinating? They are using their adductor muscles to hold up the anterior perineum, because they feel the threat of urine entering the posterior urethra and they instinctively know if that happens that the bladder will go into involuntary contraction and they will wet their pants. This function in analysis holds out very well in all types of incontinence, in many kinds of neurogenic bladders, and in cystoceles, urethroceles, and rectoceles. When there is constant leakage into the posterior urethra, the expulsive force becomes more violent, and therefore all factors toward emptying the bladder involuntarily are exaggerated, because the bladder is contracted, constantly.

WHENEVER there is urgency of urination, it means that the patient is given time to realize that he is going to lose urine if he cannot get to the toilet in a matter of seconds or minutes. When there is no urgency of urination, it means that urethral sensation is so numbed either by constant water in the posterior urethra (pressure anesthesia) or by pudic nerve change that he is not warned of urine leaking into the posterior urethra. Urgency is a symptom that without doubt decides against incontinence of the bladder, neurogenic of the atonic type.

Neurogenic bladders can vary as time goes on. Let us divide neurogenic bladders into the two general types: the spastic neurogenic bladder and the atonic neurogenic bladder. The spastic neurogenic bladder is one in which the anterior perineum is spastic, and you may expect to have hyperactive knee jerks and possibly some degree of spastic paraplegia. The atonic bladder is typically the tabetic bladder. It is one in which there is demyelination within the posterior columns; that is, the sensory side of the reflex arc is broken. What does that do? Urine is not recognized within the posterior urethra, because this sensory recognition

is carried through fibers that are carried within the posterior column of the spinal cord.

Let us say that a person has a syphilitic change in his spinal cord; he has tabes dorsalis; he does not know where his foot is; he loses sense of position in space; he is ataxic. His perineum is ataxic and anesthetized also, so he has no reflex tone to his bladder wall. The loss of tone is of the perineum—his anal and bladder voluntary sphincters are atonic. The loss of bladder tone is secondary. When sensation to the posterior urethra is damaged by demyelination within the posterior columns and urine is not recognized in the posterior urethra, there will be such a weakened reflex to the bladder wall that a residual urine will develop. Urine left behind in the bladder further breaks down the musculature by further pressure anesthesia and a vicious circle is thereby established.

LET US consider one of the most interesting complex types of neurogenic bladders. If one is riding in a closed car and has a collision, he is thrown from his seat and becomes something like a pea in a pod; he is rattled about. He may receive a severe blow on the head which would make him flaccid; his legs would be flaccid, as would his arms, neck, back muscles, etc. If he is now brought to the hospital, unconscious, drooping, he has at that moment, in effect, a tabetic bladder. He has diminished perineal tone.

If one is hit on the head with a hammer and the blow is not lethal, he will have flaccid muscles. However, if the damage to his cerebrum is not great, he will recover, but if at the time of the accident he also received an injury to his spinal cord, such as a hemorrhage or other form of irritation, he may recover with a residual spastic bladder. This will not be all; he will have spastic legs, and a spastic perineum. The spastic perineum means that he can no longer lower the internal bladder orifice voluntarily to start urination by letting water flow into the posterior urethra and so reflexly contract the bladder. He will develop a residual

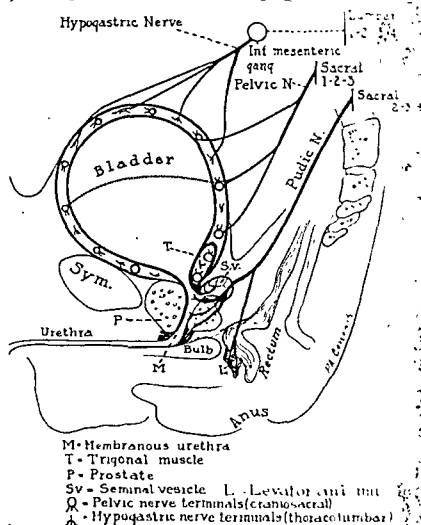


Figure 1. Diagram of the bladder wall with its trigone.

urine back of a spastic perineum, with a spastic anal sphincter.

If this young man (most such cases are boys) is catheterized when the bladder fills up, that catheterization gives him, in my opinion, about a 90 per cent mortality rate—just that one catheterization. How? It depends on whether the spastic changes in his legs and his voluntary sphincter, that is, his perineum, are permanent or not. If it is temporary, he will be all right, but if the damage to his spinal cord is such that he will remain a spastic paraplegic, he will have a permanent spastic bladder (and anal) sphincter and he will never be able completely to empty his bladder again. By catheterizing him we are going to infect him, we are going to contract the bladder wall; an infected contracted bladder kills the kidney function in one of four ways: (1) infection by lymphatic spread, (2) spread through the blood stream, (3) spread up the ureters, or (4) by back pressure, causing infected, dilated ureters

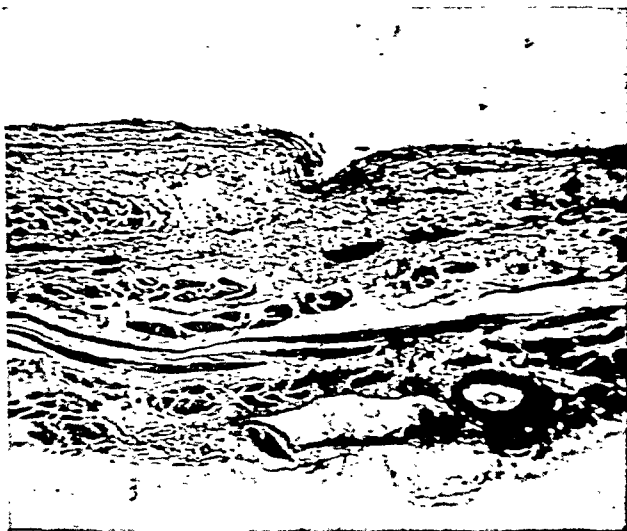


Figure 2. Normal bladder wall.



Figure 3. A compensated bladder wall showing the effect of overwork, frequent urination, and/or difficulty in forcing urine through a partially blocked outlet.

and kidney pelvis. His one hope is to develop an automatic bladder.

What could you do with him except catheterization? Nothing! Let him overdistend? Then will you kill his kidney function? Not necessarily. If he is overdistended possibly he will get an infection anyway by way of the blood stream. That is true, and if he does it is bad luck, but not poor medicine and "sufficient unto the day is the evil thereof." What would you do with him? Leave him alone and watch his breath for urinous odor, watch his NPN, and watch his general condition. Possibly cystostomy or transurethral surgery will be indicated in such a case.

In preoperative diagnosis of prostatic obstruction, we have almost given up cystoscopy. We have to employ this method occasionally, as any urologist knows. However, intravenous pyelography with a 2-hour "delayed" film will usually reveal the necessary facts, tumor stone diverticulum, and in addition will show the status of the upper urinary tract.

One of the symptoms of any urethral obstruction is a desire to void after emptying the bladder. The patient empties the bladder, but he will tell you, "I don't want to leave the toilet.

As soon as I empty the bladder, I feel that I have to empty it again." You might be surprised to find he has only an ounce of residual urine in the bladder.

This is important in that many things can be done to handle these early obstructions besides surgery, and I feel that uncalled for transurethral or poorly chosen (I prefer that term) transurethral on a physiologic basis in the early obstruction is not beneficial. I believe that about 30 per cent of all men past the age of 60 have some urinary trouble—slow stream, slow start, up at night—but they have no intention of undergoing surgery. Two ounces of residual urine is not sufficient to indicate transurethral surgery when the man is not in distress, because such surgery may leave him with an irregular urethra which may mean a permanent urethritis, which sometimes is the cause of frequency and discomfort.

Figure 1 diagrammatically shows the bladder wall with its trigone. The involuntary innervation is unimportant to us clinically. However, the pudic nerve innervating all voluntary muscles associated with micturition is, in



Figure 4. Cystogram showing a round prostate filling defect in a case of benign nodular prostatic hypertrophy.



Figure 5. Cystogram of compensated bladder wall showing the small, benign, sac-like type of prostatic obstruction of slow development.

my opinion, most important in diagnosing neurogenic bladders. The pudic nerve innervates the perineal muscles, levator ani group, and the weak compressor muscles within the urogenital triangle, as well as other perineal muscles.

Given a markedly atonic perineum in *tubes dorsalis*, for instance, the perineal muscles are atonic and allow the internal orifice of the bladder to drop from its normal and tonic upward placement, thus lowering the internal bladder orifice which tends to produce incontinence of urine. Furthermore, such a patient will void a weak stream as the bladder tone is diminished proportionately to the loss of sensation in the posterior urethra. The reason for this is that micturition is a voluntary-involuntary reflex. A person first voluntarily lowers the perineum, and *with it the internal bladder orifice*, so that urine may flow into the posterior urethra, reflexly to stimulate the bladder wall to involuntary contraction. In such a case the *voluntary anal sphincter* is correspondingly relaxed; its tone, as determined by digital palpation, is of diagnostic value in certain cases of

tubes dorsalis with dysuria, and in all atonic neurogenic bladders.

ON THE other hand, in cases of *spastic paraplegia* in which the *legs, perineum, and sphincter are spastic*, the spastic perineum elevates the internal orifice of the bladder, fixing it upward and forward in a "urine retaining" position. This patient cannot voluntarily institute voiding. He cannot release the spastic perineum, and therefore lower the internal orifice of the bladder so that urine may flow into the posterior urethra reflexly and involuntarily to stimulate contraction of the bladder wall. The spastic anal sphincter is also of diagnostic value here. However, such an anal sphincter at first palpation may be spastic and then *strictly open* to simulate an atonic sphincter. Also a relaxed anal sphincter in certain neurogenic bladders first may be relatively atonic to be stimulated into spasticity by a palpating finger. These movements by the perineal muscles influence the position of the internal bladder orifice, clinically reflected by

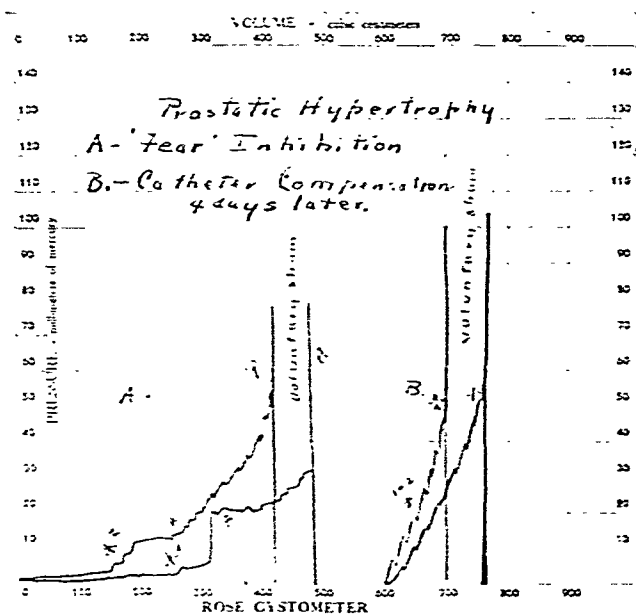


Figure 6. A cystometrogram graph which correlates intracystic pressure and bladder capacity.

symptoms of atypical retention or incontinence of urine, also the perineal muscles determine the state of the anal sphincter.

A normal bladder wall is shown in Figure 2. Back of the interdependent, voluntary-involuntary sphincter operates a smooth muscle reservoir, the bladder. Its musculature varies in thickness, with the degree of distention existing at the time that a section of its wall is made. We have in this figure a normal wall—note three layers of smooth muscle and the size of the smooth muscle bundles.

A compensated bladder wall (Figure 3) shows the effect of overwork, frequent urination, and/or a difficulty in forcing urine through a partially blocked outlet. Contraction will give thickness of wall but not such an increase in size of the muscle bundles. The time element is important in these changes. A rapidly developing bladder obstruction will not give time for bladder wall compensation as does an obstruction of slow development. Compare this bladder wall section with Figure 2, particularly the size of separate muscle bundles.

Figure 4 is a cystogram showing a round,

prostate filling defect. In this instance of benign, nodular prostatic hypertrophy, a gland of 150 gm. was removed by one-stage suprapubic prostatectomy. The bladder was not coarsely trabeculated; therefore the obstructive factors developed recently. Analysis of symptoms verified this fact. The large bladder capacity also strongly suggests recent obstruction as a thickening or compensating bladder tends to smaller capacity.

A CYSTOGRAM may serve instead of cystoscopy although the latter is more accurate; it may be chosen in instances where you wish to omit cystoscopy in cases of poor risk, hemorrhage, or a large median lobe. *If the opaque media is of the same density as the intracystic lobe of the prostate, no filling defect will be seen.*

A cystogram of compensated bladder wall is shown in Figure 5. In contrast to Figure 4, this presents the small, benign, scar tissue type of prostatic obstruction of slow development. This type, beginning early in life as a rule, gives the bladder wall time to thicken and in this instance to herniate a diverticulum through a congenital hiatus or weak spot in the bladder wall. The "neck" of the diverticulum "measures" the thickness of the bladder. We should expect to do transurethral surgery in such a case. The bladder, when relieved of its obstruction, will return to normal thickness, and I believe the small diverticulum, after operation has lessened intracystic voiding pressure, will resolve, in this instance, into a shallow cellule.

Figure 6 is a cystometrogram graph which correlates intracystic pressure and bladder capacity, and gives opportunity to place degrees of bladder filling sensations on the pressure-capacity graph.

A retention catheter, depending upon the type of bladder wall, contracts the wall either weakly or strongly, and correspondingly may abrade its mucus membrane. Also its presence in the posterior urethra offers a stimulation to contract the bladder reflexly, as urine in the posterior urethra normally effects this reaction. These reactions in a compensated bladder often



Figure 7. Cystogram of a decompensated (atonic) bladder. Note sag of internal orifice area.

result in hemorrhage, diffusion of infection, and poor drainage, the latter due to block by blood clots or edematous bladder mucosa.

This cystometrogram was made by *two usual fillings*. The asterisk 1 and 2 mark the "first desire to void," point "F" 1 and 2 the "sense of filling," and "P" 1 and 2 "pain of overdistention" in first and second curve. The first filling stimulates the bladder by stretch reflex, that is filling and emptying so that curve 2 is shorter (less capacity) than curve 1.

Through cystometric work I feel that the principle of "bladder decompression," i.e., catheter drainage before cystostomy, as applied in a poorly explained effort to protect kidney function, is not only incorrect physiology, but actually increases mortality rate in suprapubic prostatectomy.

Figure 7 is a cystogram of a decompensated (atonic) bladder wall with some regurgitation up the right ureter. Note sag of internal orifice area. Weakness is most marked at the dome and left lateral wall, but even with this the thicker portions, notably the right floor, show fairly coarse trabeculation, suggesting early long resistance to back pressure, residual urine,



Figure 8. Photograph of a section of interior of a bladder decompensated by back pressure.

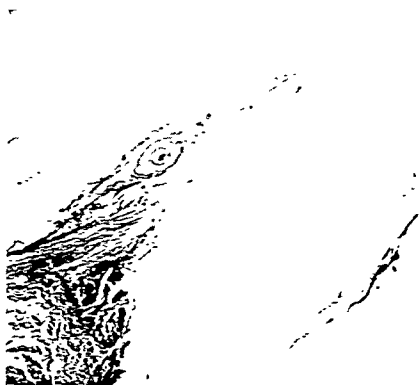


Figure 9. Cross section of a large thin-walled diverticulum.

development period, before its musculature decompensated. A tabetic type bladder would not thicken (compensate) before decompensation—it would lose strength as soon as nerve damage became progressive, and therefore would not show coarse trabeculation. This bladder has

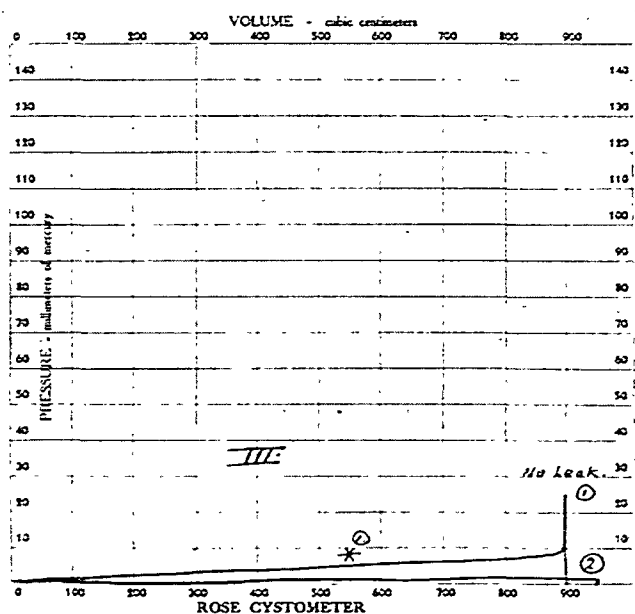


Figure 10. Cystometrogram in tabes dorsalis with large infected residual urine.

great recuperative powers, though probably not 100 per cent.

A section of the interior of a bladder, decompensated by back pressure is illustrated in Figure 8. Long years of overwork, both frequency of urination during the years when the thickening and possibly early infected bladder wall were able to overcome the prostatic obstruction, and an *increased intracystic pressure*, necessary to force urine through a partly blocked internal orifice and the prostatic urethra, produced the coarse trabeculations, diverticula, and eventual decompensation. This bladder

wall, thickened, herniated by diverticula and cellules, and even if infiltrated by scar tissue, can return to near normal function, providing the diverticula are not too large and thin-walled, in which case they will absorb a lot of the voiding intracystic pressure and a large residual urine will remain even after prostatectomy. A cystometrogram of this bladder would show large capacity, a reduced intracystic pressure, and normal sensations. The anal sphincter would be normal.

Figure 9 shows a cross section of a large thin-walled diverticulum. It requires little imagination to visualize how such a weakened area in a bladder would absorb the voiding pressure to leave a large residual urine in the bladder, as well as in the diverticulum.

A cystometrogram in tabes dorsalis with a large infected residual urine is pictured in Figure 10. This cystometrogram shows markedly diminished sensation and poor reflex innervation from the urethra to the bladder wall. The bladder musculature actually overstretches by the first filling—note that filling II is lower than filling I. The anal sphincter would be markedly relaxed. Treatment is directed toward reducing the residual urine by transurethral resection of the prostate if there is a hypertrophy or scar thickening about the prostatic urethra by manual expression of urine, by catheterization.

As a rule, catheterization of a neurogenic bladder of the spastic type is dangerous but of this low pressure, or atonic type, it is not only safe but good treatment.

The Results of Electric Shock Therapy

LELAND B. ALFORD*

ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

IN ELECTRIC shock therapy we have a method of treating the psychoneurotic states that is shorter, more thorough, and longer lasting than any other approach. The method is truly a milestone in medical progress.

I initially employed insulin for shock therapy, then metrazol, and finally electric shock. I treat a large proportion of my cases by this method, but only when I suspect that other methods might be prolonged and doubtfully effective. The cases are those of referred practice and are neither the worst forms nor the mildest. They are mostly acute or recurrent; few are of long standing.

The patients are predominantly working people who are interested in saving money and resuming their occupations. I believe that electric shock therapy is an immense contribution in both respects.

The danger of fractures and dislocations is almost completely eliminated by giving the patient two nembutal capsules an hour before treatment. The sedative action cushions the shock and complications are rare. I have had

no fractures or dislocations in my experience with this method. Occasionally the patient complains of a sore back, but it gradually disappears. I consider the dangers to be similar to those of having a tooth extracted. Advanced cardiac or coronary disease is a contraindication, but milder stages are not necessarily so.

I divide my treatments into courses, and this is a unique feature of our procedure. After a certain number of treatments the memory becomes confused, and I believe that this fact is a measure of their effectiveness. A course is the number of treatments necessary to cause this confusion. In older persons the number may be only four, while in young persons it may be as many as eight. After one course it is necessary to stop and wait about a week and to observe the patient's condition. As treatments are given daily, a course takes approximately a week.

This policy affords a certain standardization, since much time and money are frequently wasted in cases where it cannot be determined whether further treatments are indicated. Two courses are advisable and usually necessary. If there is no lasting result after three courses, the advisability of continuing with electric shock therapy is doubtful in most cases.

In the effort to minimize the expense of ther-

*Associate Professor of Neurology and Psychiatry, St. Louis University School of Medicine, St. Louis.

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LELAND B. ALFORD

apy, more and more treatments are given as out-patient procedures. The patients come to the hospitals, where beds are supplied for this specific purpose, for a couple of hours and, after the treatment, return home. In hospitalization insurance these treatments count as a day in the hospital, so no expense is incurred by the patient.

The second course, or even part or all of the first course, may consist of out-patient treatments. Occasionally patients continue to work during these treatments.

Patients over 55 years of age are likely to have recurrences within a year or even within a few months, this likelihood becoming greater as the years advance further. Little can be promised to the senile psychotic in the way of lasting results. But there is another procedure which may benefit these patients.

For some patients a regular treatment once every two weeks or every month may keep the condition in abeyance. We have employed this

method with some success and I particularly wish to emphasize it here as perhaps being to some extent unique. I do not wish to claim originality for all these different procedures because my colleagues often suggest them to me and I wish to give them credit. Dr. Deppe especially has suggested several very useful approaches, and the matter of giving nembutal to avoid fractures was suggested to me by a nurse following several disappointments with electric shock therapy.

This staggered treatment is also effective in certain paranoid and guilt complex cases, examples of which will be given, which continually recur after courses of treatments. It has enabled some patients to continue work for two years without relapses.

THIS, then, is the general procedure for all types of psychoses. I believe that the best results are obtained with the involuntional types and the poorest with manic cases. The involuntional case seems to constitute an exception to the rule that the long-standing case is unfavorable. There are instances of cases of five or even ten years' duration being relieved within the course of a few weeks and remaining well. The hyperactive manic type of case seems to relapse quickly, more often than other types, but these are only general tendencies.

It should be explained that nearly all cases improve while treatment is in progress. The unfavorable cases relapse in from one to three weeks after treatment is discontinued. If a relapse does not occur within three weeks, the effect will likely be lasting.

Recurrences in years following electric shock therapy occur as with any method of treatment. It is my impression, however, that such recurrences are less frequent with electric shock therapy than with other methods.

The neuroses are as amenable to electric shock therapy as are the psychoses. It would be a mistake to assume, however, that because they are milder, fewer treatments will be necessary. The neuroses will require as many treatments, on the average, as the psychoses

and there will be as large a proportion of failures, probably larger, because cooperation is harder to obtain. The neurotic patient seeks an easier way out. The acute phases, the acute anxiety and depression states, are the most promising types. Some schizoid neurotics will also respond with a relatively large number of treatments, but the old hypochondriac, the patient who has had aches and pains all his life, should be left alone.

In the neuroses especially much depends on the cooperation and the attitude of the patient. When he genuinely desires relief and shows that he will cooperate, electric shock therapy may be employed in many instances in which it would otherwise not be undertaken. The attitude of the family is also important. Very often an intelligent and cooperative member of the family will determine the success of the procedure.

I believe there are many such cases of neuroses which will never yield to any other type of therapy and therefore electric shock should be kept in mind as an expedient if it can be applied successfully.

I would say in 4 out of 5 cases, or at least 3 out of 4, of psychoneurotic illness, electric shock therapy is a boon. It relieves many who otherwise would get little if any relief. The relief is more thorough and longer lasting; the length of treatment is greatly reduced, often from months to weeks or even days, and the cost and loss of time are likewise lessened.

There still remains the case that responds and quickly relapses. I am unable to predict these cases. One can speak only of percentages. Continually, cases which seem favorable turn out not to be so, and conversely cases that appear unfavorable respond favorably. Even after having given from 1,500 to 2,000 treatments a year since this therapy was first employed, I still cannot predict whether a patient will respond or not. It is not possible to divide the cases into types and to predict by types what the result will be.

This does not apply, however, to the frank chronics, the cases with hallucinations or the long-standing cases where the prognosis is poor

and treatments are given only with some definite purpose in view such as quieting the patient. Some patients require treatment either in a sanitarium or by a systematic approach; their conditions cannot be corrected quickly.

How can electric shock therapy be made to reach these resistant cases? I do not know. I have tried increasing the number of treatments; occasionally this system gives good results. I have tried giving treatments beyond the confusion stage, but it is difficult to continue treatments when the patient becomes almost blank. Perhaps such expedients should be investigated further. One such expedient I will mention again later.

Frontal lobotomy for the unfavorable case is, of course, one recourse, and I have tried it in about 40 cases. Fifty per cent or more of these have had fairly favorable results, some of them brilliant.

IF ELECTRIC shock therapy proves ineffective, I will the patient be worse off than before? I do not think so. He may be somewhat more active and resistant, but any difference is basically not important. I do not believe there are any permanent harmful results.

There are one or two incidental uses of electric shock therapy. A rather surprising one is in the treatment of general paralysis due to syphilis of the central nervous system. The violent parietic will be subdued by electric shock therapy and rationality will often be restored. I have given parietics electric shock therapy in the hospital until they were restored mentally, and then carried out a course of malaria in the home. My experience with such cases has not been extensive, however.

Another use of electric shock therapy is that following frontal lobotomy where there is incomplete recovery or recurrence of symptoms. Electric shock therapy apparently is more effective after the operation. However, more frontal lobotomy cases have had the benefit of shock therapy before the operation.

The method of staggering treatments has another effect. When symptoms continually re-

cur after courses, I have resorted to the method of having the patient go home, giving treatments at regular intervals, and continuing this indefinitely. Some of these patients continue with their work, with the understanding that they will come in once every month or once every three weeks for treatment, whatever their condition is. In some cases this procedure has been employed for two years.

CASE REPORTS

Eugene had a guilt complex; he washed his hands a lot and did a lot of praying; he would have spells of panic and think he was going to die or go crazy; and he was very nervous and sleepless. He was in the hospital for several extended periods undergoing electric shock treatment. During one period he sought solace in alcohol; we tried to shift to sedatives, but Eugene was apt to drink the whole bottle of sedative at one time.

Finally we came to the point where we were giving treatments periodically, perhaps once a week to start, once every two weeks, then every three or four weeks.

His mother died in the meantime, but first she had a fracture of the hip, was in bed for many months, finally had strokes and died. Then there was an unfortunate love affair.

Eugene has now been working regularly for a couple of years. How long have you been working?

PATIENT: About 17 months.

DR. ALFORD: Instead of spending money he has been earning money and helping the family out. How are you getting along, Eugene?

PATIENT: Very well now, Doctor, I believe.

DR. ALFORD: Are you sleeping well?

PATIENT: I don't have any trouble sleeping at all. I sleep very well.

DR. ALFORD: No more drinking?

PATIENT: No, no more drinking, none whatsoever.

DR. ALFORD: Not very much praying?

PATIENT: Not so bad; I don't pray nearly so much any more.

DR. ALFORD: Next is Martin. The Nazis got after Martin. They first closed in on him in a

New York hotel and there was quite a commotion. He got home and had several courses of electric shock therapy, but the idea kept coming back. Finally we switched to the method of staggering treatments. You get one every three weeks?

PATIENT: Every month, now.

DR. ALFORD: He was in a war plant at that time. When that closed down he went to work as a draftsman, and practically ever since the close of the war you have been a draftsman?

PATIENT: Since I left the university. I was trained in the university as an architect.

DR. ALFORD: How long is that?

PATIENT: I graduated in 1936.

DR. ALFORD: Since the war you have been working with private firms?

PATIENT: Yes, a couple of years.

DR. ALFORD: You are working regularly?

PATIENT: Yes, working every day, five days a week.

DR. ALFORD: Do you feel pretty well?

PATIENT: I am feeling a lot better.

DR. ALFORD: You have been feeling better the last two or three months?

PATIENT: That is right.

DR. ALFORD: I do not think this procedure of staggering treatments is altogether a temporizing one. I think it may be one method of approach. I recall one case that I was very worried about in which a voice—an auditory hallucination—persisted. Despite courses of electric shock, the girl could hear this whisper all the time.

In desperation I put her on these staggered treatments for several weeks, then every two weeks, then every three weeks, and after about eight or nine months, to my delight, she told me one day she had not heard the voice for a couple of weeks. Now the treatments have been discontinued altogether.

In conclusion, electric shock therapy, I believe, is a great boon in the care of the psychoneurotic patients and even has brought relief to otherwise incurable cases. I also think it is possible that the method of staggering treatments in the form of out-patient treatments is perhaps a useful approach.

Glomerular Nephritis: Recognition and Treatment

FRED I. GILBERT, JR., M.D., AND L. MARTIN GRIFFIN, JR., M.D.

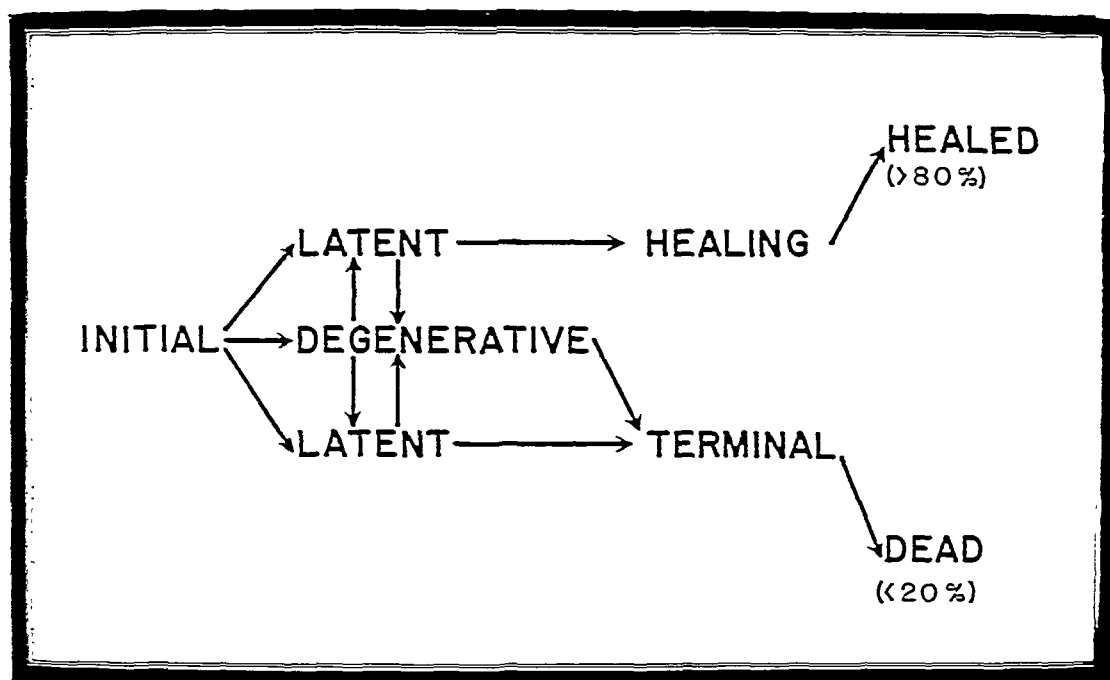
DEPARTMENT OF MEDICINE, STANFORD UNIVERSITY SCHOOL OF MEDICINE, SAN FRANCISCO

ALTHOUGH we know little of the prevention of glomerular nephritis and have only hypotheses as to its pathogenesis, it is nevertheless true that some progress has been made in the recognition and management of the various stages through which the disease develops.

Treatment of glomerular nephritis involves imposing the least possible work on the damaged kidney. Experimental and clinical evidence indicates that when a large number of nephrons have been rendered wholly or in part functionless, a reduction in the osmotic work of the kidney decreases uremia, anemia, hypertension, and proteinuria. Reducing the renal work is accomplished by decreasing the protein intake to a low but adequate level.

The diagnostic and therapeutic principles included in this exhibit are those that have been developed and put into practice by the group engaged in the study of Bright's disease at the Stanford University School of Medicine.

Medical Illustrations: The Heart, Vol. 2, Herring, and Fennell, Drawing of Blood, 7. Dr. J. H. Harrison, Stanford University. Photographs of certain renal sections from "The Renal Lesions in Bright's Disease," HARRIS, T., and GRANT, J. B. E. Hoeser, New York, 1931, and others from "Glomerular Nephritis: Diagnosis and Treatment," HARRIS, T. The Macmillan Company, New York, 1931.



DEFINITION

A pan-nephritis believed to be caused by an antigen-antibody reaction following an infection by hemolytic streptococci, and characterized by a changing clinical picture dependent on the progression of the glomerular, tubular and interstitial lesions.

INCIDENCE

Less than 1% of patients with hemolytic streptococcal infection will develop glomerular nephritis. Abrupt onset of glomerulitis occurs within one month after infection. Seventy per cent of cases are between the ages of 5 and 20 years, although no age group is spared.

Of those patients developing glomerular nephritis, over 80% will undergo healing. Of these, 80% will be healed in two years; the remainder within ten years.

CRITERIA OF HEALING

1. Absence of red blood cells in acid, concentrated urine.
2. Less than 200 mg. proteinuria per 24 hours.

DIAGNOSTIC STEPS TAKEN WHEN PROTEIN IS FOUND IN THE URINE

A thorough history and physical examination should precede any laboratory investigation.

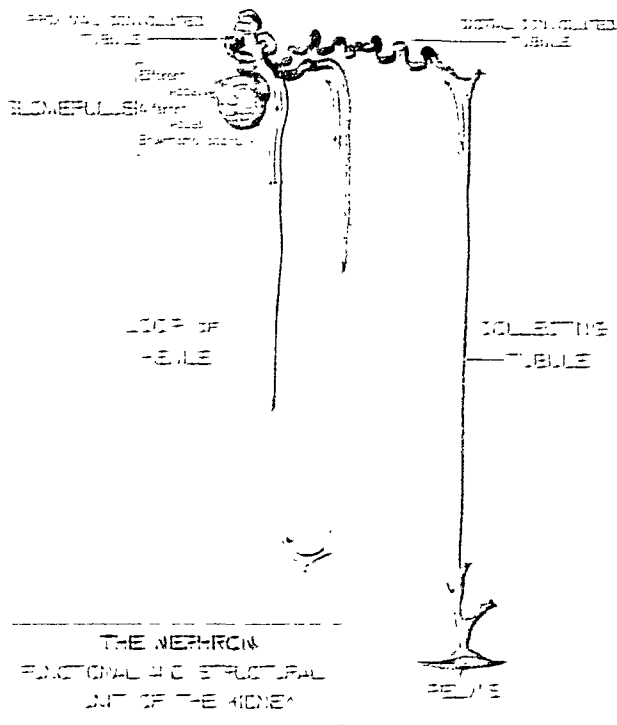
1. Repeat urinalysis with sediment study on a fresh specimen (formed elements, cells, bacteria).

Blood studies include white cell count, packed cell volume, sedimentation rate, and serum creatinine.

2. Appropriate bacteriologic studies, depending on clinical picture and sediment.

3. If serum creatinine is less than 3 mg. per cent, concentrate the urine for a twenty-four hour protein excretion, and an Addis count of cellular elements and casts. If creatinine is greater than 3 mg. per cent an attempt to concentrate urine will cause an increase of uremia.

4. If urinary findings, history, and physical examination suggest lesion other than glomerular nephritis, residual urine and excretory urograms may be done to aid in the exclusion of neoplasms, congenital anomalies, and chronic pyelonephritis. Cystoscopy and retrograde pyelography are done if necessary.



COURSE

The patient who contracts glomerular nephritis may pass through the following stages:

INITIAL stage **STAGE 1** the patient must be glomerular nephritis. In this stage a *moderate* improvement.

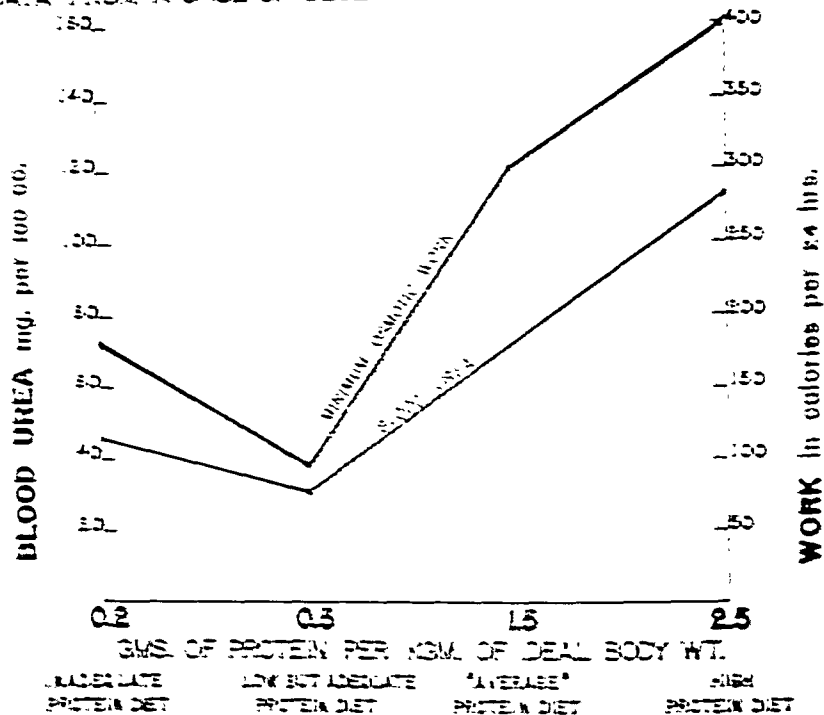
Initial stage rapidly advances and patient usually passes into the **asymptomatic LATENT STAGE**.

A small percentage pass into the **DEGENERATIVE** **STAGE** readily recognized by patient and doctor.

As the lesion progresses and the number of functioning nephrons decreases, the patient gradually slips into the **TERMINAL STAGE**.

MINIMUM OSMOTIC WORK OF THE KIDNEY: AT VARIOUS LEVELS OF PROTEIN INTAKE.

(DATA FROM A CASE OF DEGENERATIVE GLOMERULAR NEPHRITIS)



MINIMUM OSMOTIC WORK OF THE KIDNEY AT VARIOUS LEVELS OF PROTEIN INTAKE

It will be noted that blood urea and osmotic work increase directly with the protein intake, except where an excessive protein diet results in increased catabolism of body protein.

(Data from a case of degenerative glomerular nephritis)

TREATMENT

RATIONALE OF LOW BUT ADEQUATE PROTEIN DIET

Allowing the diseased kidney to rest is the most effective therapy. This is accomplished by reducing osmotic work. The minimum osmotic work (W) of the kidney in excreting each urine volume for 24 hours is expressed in the formula:

$$W = NRT \left[1 - \frac{U.C.}{B.C.} - \left(\frac{U.C. - B.C.}{U.C.} \right) \right]$$

Where N = Rate of excretion in gram moles / 24 hours.

R = Gas constant.

T = Absolute temperature.

$U.C.$ = Urine concentration of solute.

$B.C.$ = Blood concentration of solute.

W = Work in calories / 24 hours.

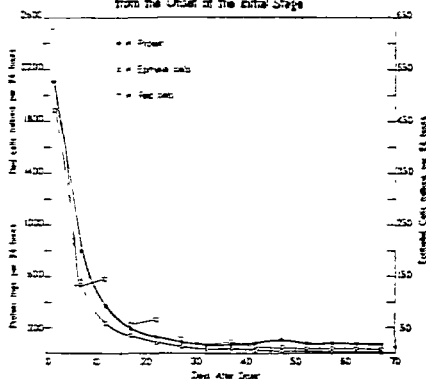
Therefore urine volumes with high excretion rate (N), and a high $\frac{U.C.}{B.C.}$ ratio require considerable work to excrete. Urea is the only solute where both conditions exist.

THERAPEUTIC CONCLUSIONS

1. Urea excretion should be kept at a minimum by adequate low protein diet.
2. Urine should be kept dilute at all times.

THE BEST TREATMENT OF GLOMERULAR NEPHRITIS

Rates of Excretion of Protein, Red and Epithelial Cells from the Onset of the Initial Stage



Initial Stage

Bed rest at least one week.

Low protein diet (most important during this stage as reducing the excretory work may permit recovery of a larger number of nephrons than would occur with high protein diet).

Latent Stage

Low protein diet as long as active disease continues (or longer because of nephron loss). Lead normal life.

Calculation of Adequate Low Protein Diet

Adults: Give $\frac{1}{2}$ gram of protein per kilogram of body weight daily, plus protein lost in urine per 24 hours.

Children: $\frac{1}{2}$ to 1 gram of protein per kilogram of body weight daily, plus protein lost in urine per 24 hours.

Degenerative Stage

Low protein diet, plus protein lost in urine.

Salt restriction to reduce edema.

Periodic relief of symptomatic effusions by paracentesis, thoracentesis; Southey tubes where edema fluid is mobile.

(Large amounts of serum albumin or plasma intravenously induces diuresis in many patients, but causes only transient rise in plasma proteins. Other diuretics may be harmful.)

Terminal Stage

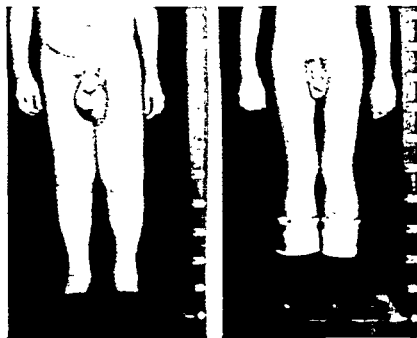
Low protein diet.

Increase salt (depending on cardiac status) to prevent dehydration.

Replace loss of fixed base.

Transfusions for symptomatic anemia.

Terminal symptomatic care.



Patient in degenerative stage of glomerular nephritis with massive mobile edema. Southey tubes inserted in distended tissues of legs resulted in loss of 3,500 cc. of fluid in six hrs., 45 lbs. weight loss in five days.

CLINICAL PATHOLOGICAL STAGES

INITIAL STAGE



Symptoms and Signs

Abrupt onset of
Coffee- or red-colored urine.
Moderate hypertension.
Brawny edema.

Appearance of Urine

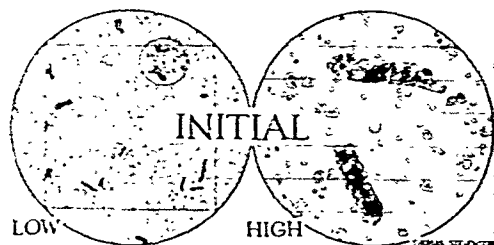
Opaque brown or red.
Urine Protein
Proteinuria of 0.2 to 3.0
gm./24 hours.

Hemo-Chemical

Serum creatinine elevated. Mild anemia and hypo-
proteinemia (due to increased blood volume?).
Leukocytosis. Rapid sedimentation rate.

Renal Function

Moderate to severe temporary impairment due to
blockage of large number of glomeruli.

Most Important
Sediment
Findings

Red cells, red cell
casts and many tu-
bule cells.

Pointer indicates red blood cell cast in lu-
men of tubule. Above are fresh RBC with-
in tubules.

LATENT STAGE



Symptoms and Signs

The only abnormalities found in this stage are in
the urine.

Asymptomatic.

Appearance of Urine

Clear.

Urine Protein

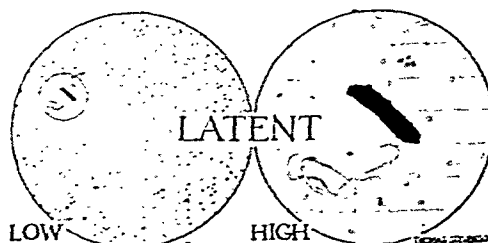
Usually less than 0.5 gm./24 hours.

Hemo-Chemical

Serum creatinine usually normal. No anemia, leu-
kocytosis. Plasma proteins normal. Sedimentation
rate usually elevated.

Renal Function

May have 10-60% reduction in function due to ir-
reparable loss of nephrons.



Most Important Sediment Findings
Persistent microscopic hematuria and red
cell casts.

OF GLOMERULAR NEPHRITIS

DEGENERATIVE STAGE



Symptoms and Signs

Feels well except for pitting edema of ankles and face at onset; later may develop mechanical discomfort from ascites, hydrothorax.

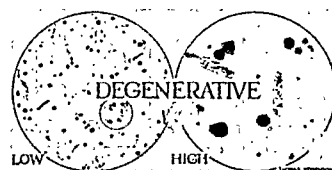
Appearance of Urine
Clear, foamy.

Urine Protein
Marked proteinuria of 5 to 50 gm./24 hours.

Hemo-Chemical

Serum creatinine normal at first. Hypoproteinemia. Lipemia with elevated blood cholesterol.

Renal Function Decreasing renal function.



Phase microphotograph. 1. Hyaline cast with fat and epithelial cell inclusions. 2. Epithelial cell filled with fat. 3. Hyaline cast. Tubule cell.



Most Important Sediment Findings
Droplets of fat in casts, in epithelial cells and free in the urine. Microscopic hematuria.

TERMINAL STAGE



Symptoms and Signs

Development of fatigue, nausea, vomiting parallels increasing uremia with anemia, hypertension.

Appearance of Urine
Pale, clear.

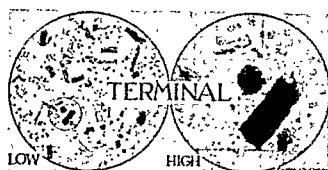
Urine Protein
Moderate proteinuria of 3 to 15 gm./24 hours.

Hemo-Chemical

Serum creatinine high. Increasing anemia. Low or normal plasma proteins (5 gm.).

Renal Function

Majority of nephrons destroyed, deepening uremia.



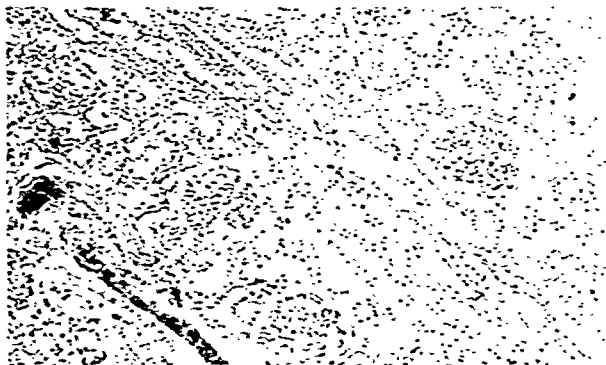
Fragile renal failure cast. Broad casts in ducts of Bellini at entrance to renal pelvis.



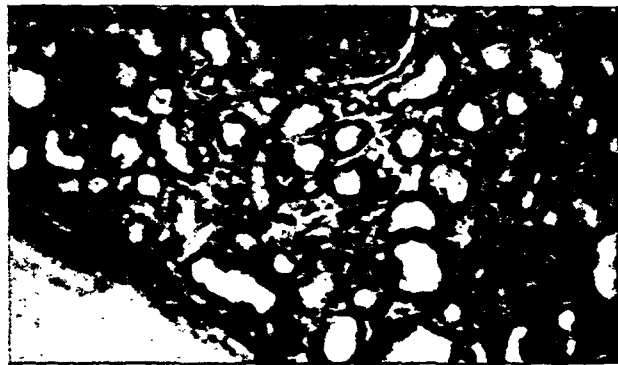
Most Important Sediment Findings
Even with dilute urine, RBC are found. Number and breadth of broad casts increases with slightest dehydration.

TISSUE SECTIONS

In all stages of glomerular nephritis, the clinical picture equals the sum total of the interdependent glomerular, tubular, interstitial and vascular lesions.



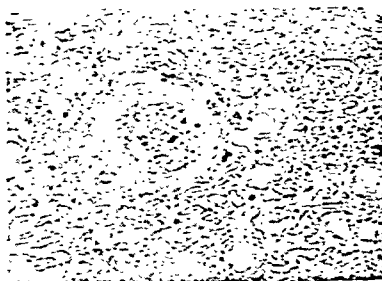
Normal—Kidney section showing normal cyto-architecture of glomeruli, tubules, interstitial tissue and vessels.



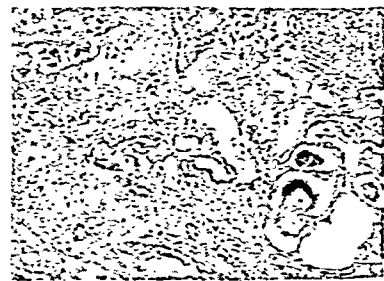
Degenerative stage. Sudan stain shows much fat in tubule cells.



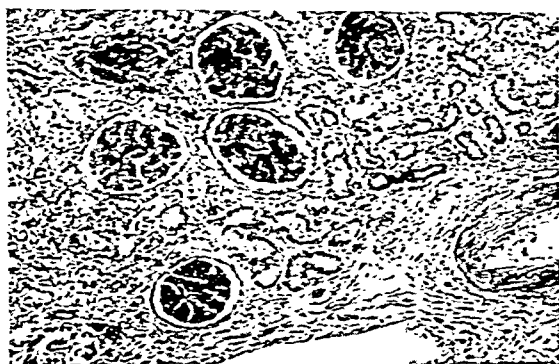
Expired during initial stage. Stormy clinical course with death one month after onset. Age 5. Striking epithelial crescent in center of field, tubular atrophy and dilatation, and granulocytic infiltration are compatible with the short clinical course.



Expired in terminal stage. Age 38. Many shrunken, fibrotic glomeruli, glomerulus with extreme pericapsular fibrosis, epithelial crescent and fibrotic tuft, alternating tubular dilatation, interstitial scarring and arterial thickening.



Terminal stage. Extreme cyst-like dilatation of tubules alternating with atrophied or compressed units, possibly due to interstitial scarring.



Expired during latent stage. Age 45. Only evidence of renal lesion is cellular increase in glomerular tufts, some cortical scarring and intimal thickening.



Expired at end of degenerative stage. Kidneys large and smooth. Dark tubule cells and some glomeruli contain much fat. Age 45.



The Medical Bookman

PHYSICAL MEDICINE IN GENERAL PRACTICE*

THIS is the second edition of Dr. Bierman's important work on physical therapy in medical practice. World War II demonstrated effectively the value of physical methods in medical and surgical practice with rehabilitation on a large scale in speeding the recovery of the wounded and those ill from other causes. Dr. Bierman has included this valuable material in his new edition and has added a chapter on specific problems of rehabilitation which are of interest to the medical practitioner. There is still relatively little general use of these extremely valuable adjuncts in aiding people to recover from disease and injury, and with the new emphasis upon early ambulation in both surgery and medicine, this phase of practice is increasingly important. A book such as this naturally then becomes important to the general physician who would keep himself and his practice in accord with the most modern thought. The organization of the subject matter and the approach to it is everywhere kept within the viewpoint of the general practitioner.

Heat and cold are still the most widely used physical agents, and the most valuable. A considerable proportion of this book is devoted to these agents. "The skin may be considered as an organ which lies between the interior of the body and its environment. . . . The blood vessels of the skin form a large reservoir capable of holding about one quarter of the total blood volume, which increases or diminishes markedly in accordance with local and general needs. . . . Changes are also brought about through the action of nerves and nerve endings, lymph channels, sebaceous and sweat glands, and by metabolic responses, such as pigment for-

mation and production of vitamin D. . . . These and other changes occurring in the skin are of particular importance in explaining the therapeutic value of many physical procedures whose influence is completely or mainly limited to the integument."

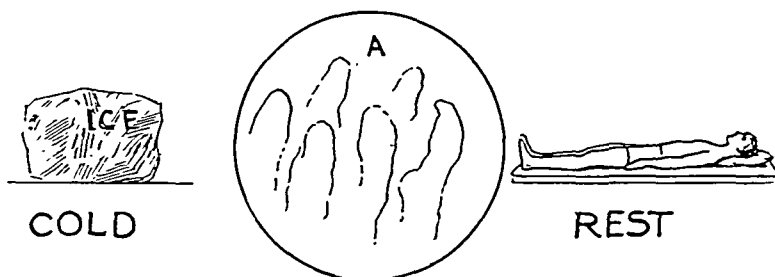
The author further discusses the use and effectiveness of heat and cold when applied to various parts of the body and the specific uses to which they can be put. The anesthetic effect of cold is pointed out, as well as possible dangers which it may cause. Particularly dangerous, of course, is the use of the ice bag in abdominal pain liable to be caused by an inflamed appendix, when the diminished sensitivity may cause a false sense of security, while the infection proceeds to a dangerous point. Also mentioned is the shocklike condition produced on some people by immersion of even the hands in cold water, with actual syncope at times. The use of cold to diminish the blood needs of extremities in which the circulation is impaired by injury is discussed. Indications, value, and technic of heat application is also effectively presented.

Hydrotherapy, both local in the recovery and rehabilitation of injured extremities, and general in more widely spread muscular damage such as that from poliomyelitis, is the subject of an entire chapter. Typical of the author's attention to practical detail is the description of the lowly Sitz bath, a most effective form of relief in the ever-present ano-rectal disturbances, and the continuous hot compresses in treating infections of the skin and subcutaneous tissues.

The effect of climate upon health is the subject of a chapter, including the various physiologic effects produced by heating and chilling. Of climate in general, the author states: "The most beneficial influence of climate would be secured when living

*Physical Medicine in General Practice. By William Bierman, M.D. (With a chapter on medical rehabilitation by Sidney Licht, M.D.) 686 pages. 1948, Paul B. Hoeber, Inc., New York. Price \$8.00.

VASOCONSTRICTORS



VASODILATORS

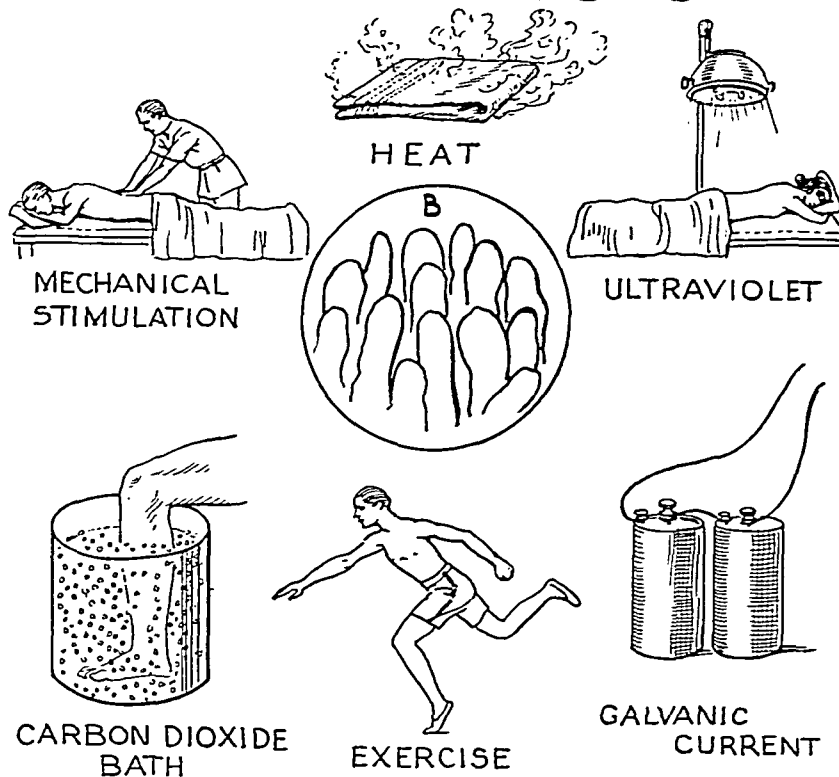


Figure 1. Physical agencies causing vasoconstriction and vasodilatation. A. Constricted capillaries. B. Dilated capillaries (schematic). (Illustrations from Bierman: *Physical Medicine in General Practice*.)

Figure 279. Buerger exercises. Position A: Legs held elevated.

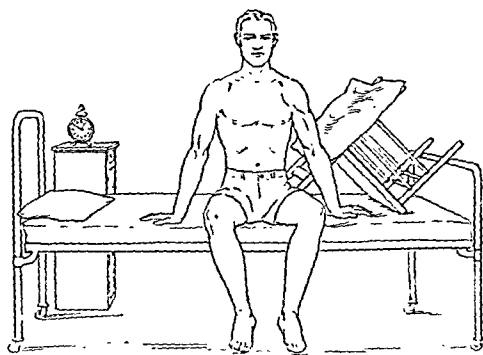
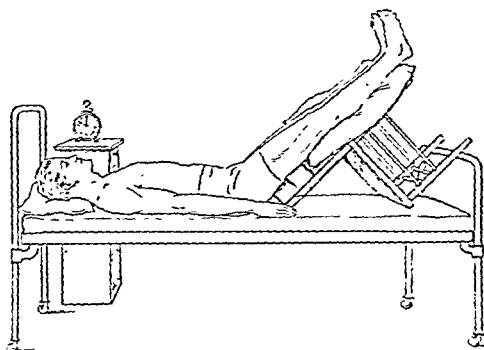
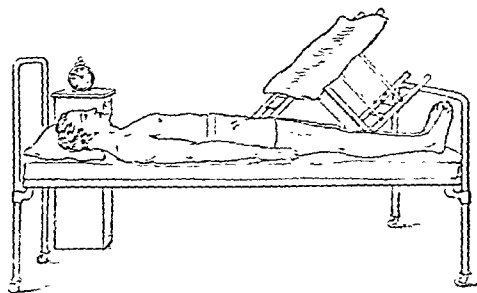


Figure 280. Buerger exercises. Position B: Patient sitting on edge of bed.

Figure 281. Buerger exercises. Position C: Patient lying flat on bed.



outdoors in a comfortable environment wearing little, if any, clothing." He continues to point out that climate has largely been discarded as a factor in the recovery from tuberculosis and that the high, dry climate formerly favored may actually be dangerous because of oxygen lack. Continuing further, the author discusses the beneficial effect of rest and change in spa therapy upon nervous tension disorders, probably the greatest benefit that climate has in treating human ills. In concluding this chapter, the attributes of most well known American Spas are mentioned.

MANY OF the muscular strains which come to the general physician are markedly benefited by "baking" with radiant heat, and since high pressure instrument salesmen are always waiting to place expensive instruments with the unwary physician, Dr. Bierman's advice in regard to this form of treatment is valuable. "The carbon filament lamp, modest though its appearance and price, lowly though its position (from the medical practitioner's point of view because it is offered for sale to the layman by druggists, hardware and department stores), is none the less an extremely useful instrument. It deserves a place in every doctor's office, in every hospital, and for that matter in every home, because of the numerous conditions in which it may be of service. . . . Deserving of extensive use in the physician's office and in the hospital is the tungsten filament lamp which is comparatively richer in visible radiation and emits a far whiter light because of the metal used in it." The dangers of this form of treatment are also described, something which every physician using any physical method must keep constantly in mind.

Diathermy, both the long-wave and the more frequently used short-wave forms, has proved of much value in treating a widely varied number of conditions. A great deal of misconception seems to exist in regard to its beneficial effects and Dr. Bierman says: "Whether or not any effect other than of heat is produced on animal tissues by the short wave current is a contraversial question. . . . The opinion held today is that a special non-thermal effect is not exerted by the short wave current." Keeping this in mind, it is obvious that for

many of the conditions treated by the general physician, such expensive machines are neither necessary or safe, and Dr. Bierman says further, "Short wave diathermy should not replace simpler forms of heating that are equally effective." The chapters on diathermy, however, are complete and authoritative for those who need to use this method.

"Give me power to produce fever, and I will cure all disease," an aphorism attributed to Hippocrates, is quoted in the opening of a chapter on Fever Therapy. Various methods of producing temperature elevation as a therapeutic measure are discussed, but with the diminishing need for fever therapy in venereal disease and the expense and special knowledge required to apply it, the general physician will probably not be much concerned with this form of treatment. There is an excellent chapter on Fever Therapy, however, as well as on Surgical Diathermy and the use of the Galvanic Current in the diagnosis of nerve injuries and in stimulation of activity in muscles during nerve regeneration.

Perhaps no form of physical therapy is more widely misused than heliotherapy, both by exposure to the sun and with ultraviolet lamps. Its use has been shown in many cases to be positively dangerous for the tuberculous and this is sometimes true of other conditions. As to the actual value of ultraviolet radiation, there is considerable difference of opinion and perhaps the simplest and most effective answer is Dr. Bierman's: "After ultraviolet radiation the patient has a healthier appearance; his skin has a better texture; his muscles are firmer; psychologically there is no doubt that a person who can see a mild erythema and subsequent pigmentation of his skin feels better because of his healthful appearance."

An important physical measure often overlooked by the general physician is massage. This is particularly true, also, since the newer work on emotional influences in psychosomatic medicine has shown the importance of the physician-patient relationship in psychotherapy. Dr. Bierman says pointedly: "The psychological factor of which many physicians are probably unaware, offers an explanation for the widespread activities of irregular practitioners. The physical 'laying on of hands' has a reassuring value, even though these hands

be not guided by honest and scientific reason." And in view of the widespread use of massaging machines in beauty parlors and the extravagant claims made for them it is interesting that "Contrary to popular belief, massage does not directly increase muscle power nor does it remove fat. When Rosenthal massaged the abdominal walls of animals with sufficient vigor to produce multiple hemorrhages, destructive changes in adipose tissue were not observed."

"Rehabilitation should begin as early in convalescence as the course of the disease will permit, but too often in the past a well intentioned caution on the part of the physician has delayed its commencement beyond the point of maximal advantage," states Dr. Sidney Licht in his excellent chapter on Medical Rehabilitation.

The tremendous value of early rehabilitation with graduated exercises and occupational therapy was so well demonstrated by our experience during the recent war that every physician should familiarize himself with what can be accomplished and, more important, the extreme importance of beginning early, before unsatisfactory habit patterns are formed. As Dr. Licht says: "Medical rehabilitation will increase in importance with the passage of time if for no other reason than that it will eventually save the community and the state much money which would otherwise be spent in unemployment benefits, insurance compensation, and custodial care." This one chapter will be well worth the price of the book to the average physician, if it enables him to get both surgical and medical patients back to normalcy in a shorter period of time.

"The physician assumes legal responsibility when he treats patients by physical agents just as he does when he employs chemical agents. He must therefore exercise reasonable professional care

in the treatment of his patient. This includes taking a history and making a physical examination. When an unusual form of treatment is used the physician assumes an additional risk because, if any accident occurs, the plaintiff may contend that this ministrations differs from accepted practice." This statement should give pause to those using physical therapy instruments with which they are not wholly familiar and points up again Dr. Bierman's often repeated thesis that the simplest form of physical therapy is the best.

THE LAST third of the book deals with specific disease conditions in which physical therapy is of benefit, with a discussion of the type of treatment liable to prove most effective in each. Indicated procedures are given in detail as to technic, including the exercises, etc., necessary for rehabilitation. Dr. Bierman also points out the importance of such treatment in the neuroses which constitute approximately half of medical practice with: "For neurotic and psychically disturbed patients, physical procedures are of value not only because of the physiological changes which they induce, but also because of their psychological influence. Weir Mitchell first called attention to the fact that neurotic patients require a definite treatment regimen of rest, dietary advice, and physical therapy."

Physical Medicine in General Practice is a complete and authoritative book on this important subject. It deserves study by all those who plan to use physical methods, which in the essence means every physician, for modern experience has shown that proper rehabilitation is as important as any other form of therapy in the treatment of both medical and surgical conditions.

F. G. S.

MEN OF MEDICINE

Lahey. Perfectionist

FRANK HOWARD LAHEY, distinguished surgeon, founder and driving force of the Boston clinic that bears his name, is a perfectionist. His colleagues recognize the fact, and his friends—whether trying to match his mid-eighties score on the golf links or participating in field trials of hunting dogs—confirm the diagnosis. Psychologists and psychiatrists have made us wary of the term, but Dr. Lahey exemplifies that *rara avis* a perfectionist who constantly drives himself and his staff to new heights of excellence, and yet remains disciplined, controlled, without frustration or inner struggle. He is a man confidently working in one direction, devoted to the clinic and its ever increasing usefulness, devoted to his wife, content with a strenuous regimented routine. He is a man who lives the life he wants, is convinced of its worth, has fun doing it!

Such inner peace results from a combining of many qualities, among which courage and clear-headedness are outstanding. It took extraordinary courage for young Francis Lahey (disliking the baptismal form of the name he changed it to Frank during his Harvard student years) to reject the place long prepared for him in his father's bridge building firm, and to pursue his determination to become a surgeon. The decision was the more difficult because the construction firm of Fletcher and Lahey was prosperous, well respected, ready for the sons of both partners to carry on what their fathers had so ably initiated. Moreover Frank had definite engineering ability. Against all that, he could offer only the unsubstantiated conviction that he wanted to be a surgeon. He couldn't argue his case logically; he didn't know why. Probably modern vocational experts who maintain that both surgeons and engineers need the quality of "structural visualization" would assure him that

surgery has effectively utilized his native ability. And no one who observes the precision and efficiency with which the clinic is run could deplore that his business talents have not found an outlet.

After the event, it is easy to rationalize, and today Dr. Lahey generously attributes his interest in surgery to Dr. Charles Benson of his home town, Haverhill, Massachusetts. He was, says Dr. Lahey, "a man well trained and well in advance of his time . . . with whom I was closely acquainted and whose work I watched before studying medicine."

He took his M.D. degree at Harvard Medical School in 1904, thereafter serving as intern and house surgeon at Long Island Hospital. From 1905 to 1907 he acted as surgeon at the Boston City Hospital, and later at the Haymarket Relief Station. In 1908 he was appointed Instructor in Surgery at Harvard, and continued to hold positions there until he changed to Tufts Medical School, where he became Assistant and then full Professor of Surgery, a place he held, with time out for service at Camp Green and overseas during World War I, until 1917. On his return from France he was made Professor of Clinical Surgery at Harvard with teaching in the Boston City Hospital.

He was still a very young man, he had vindicated his choice of profession, he was doing extremely well. But boyish-appearing Dr. Lahey had experienced enough of two kinds of medical practice to feel stirring within him that urge to perfection that is still characteristic of him at sixty-seven. He had been accustomed to spending part of his day operating at City Hospital on charity patients, i.e., on X23, Z7, Y46. Then another part of the day he would spend working with private patients, Maribel Knox, Arthur Sinton—real people, individuals recognized as such, deserving of the encouragement and the help that can flow



FRANK HOWARD LAHEY



SARA M. JORDAN, M.D.

from the doctor-patient relationship. Worried young Dr. Lahey wanted all his patients to be individuals with names, not anonymous cases with numbers. Moreover he realized that sick people usually need more complete care than any one man, no matter how humanly sympathetic or how talented, can give them. And so, tentatively at first but with high hope and firmly rooted ideals, the idea of the clinic evolved.

Sitting in his modestly furnished but attractive office at the clinic today, overlooking the stream of traffic on Boston's Commonwealth Avenue, Dr. Lahey may disclaim all knowledge of how it really got under way, how it grew so amazingly that the original building erected on the present site in 1926, was doubled in 1933, again doubled in 1939, and is currently once more being enlarged. He may say that he just can't account for how it all

happened, but he remembers the courage it took to resign a Harvard professorship for a dream of increasing the numbers of sick people who could be treated sympathetically as human beings, and yet who would have at their service the complete care of a staff of skilled experts.

His own role Dr. Lahey sums up in the sentence: "I am a fairly good surgeon and not much else." But those who know attribute a large part of the clinic's success to the personality of its founder. One of those who has most reason to know is Dr. Sara Murray Jordan, the charming gray-haired woman who is chief gastroenterologist at the clinic. As a young medical student at Tufts she had done metabolism work for Dr. Lahey when he was a professor there, and when the idea for the clinic finally took shape she was asked if she'd like to continue it with the new group that was being formed. She became a part of that nucleus that included, along with herself as youthful pinch-hitter, Dr. Lincoln Fleetford Sise, anesthesiologist, and Dr. Howard M. Clute, an assistant until 1935. Her recollections of those early days are full of Dr. Lahey's inexhaustible kindness particularly toward the very old and the very young.

"My daughter, who's grown up now," Dr. Jordan inclined her head toward the silver-framed portrait of a handsome young woman, "says she has never known greater gentleness than Dr. Lahey's when he treated her for swollen glands when she was four. Sometimes I was afraid that his kindness would lead patients into speaking of him without the respect he deserved. I remember I once reproached an old woman for saying to me, 'Lahey doesn't think so.' When I frowned at her disapprovingly, she said indignantly, 'Well, I don't say Mr. Shakespeare, and I guess that they're both tops.'"

And if Dr. Jordan's affectionate respect for her friend, guide, and chief was deeply rooted, Dr. Lahey's respect and admiration for her ability took definite form. Twenty years ago he had her treat him for stomach ulcer, observing the rules so meticulously that he even drank milk while operating. It was only when he went up to Rockport for a recuperative vacation after the peptic ulcer had healed that he found occasion to remonstrate with his doctor. Having played eighteen holes of

golf the first morning, he dragged back to the club house limp and perspiring. "Say, do you realize how weak people are after your treatment?"

AS A MATTER of fact it speaks well for both doctor and treatment that the patient suffered no recurrence, not even in the clamor and strain of wartime Washington in the early 40's where Dr. Lahey was chairman of the Service for the Procurement and Assignment of Medical Personnel for all of the Armed Forces. Indeed, being by temperament and training an essentially controlled and disciplined person he actually throve on the overwork that drove most men into fury and frustration. He sums up his notable achievement with characteristic, dry brevity. "With the aid of the other members of this board, Drs. Harvey Stone, Harold Diehl, Willard Camalier, and James E. Paullin, [we] organized, set up, and oversaw the program for obtaining medical personnel for the Armed Forces without unduly dislocating medical care." So competently did he handle this task that he was also appointed chairman of the Medical Consulting Board of the U.S. Navy in which capacity he "visited and inspected nearly every naval institution maintained by the U.S. Navy" with special emphasis on "inspection tours in the Pacific before many of the large undertakings" in the Pacific theatre of war. As an additional duty he and his clinic trained large groups of Navy surgeons in the use of spinal anesthesia.

As it happens Dr. Lahey is an experienced and enthusiastic traveler, making use of all known methods of transportation but delighting particularly in airplane travel. Often he utilizes necessary trips not only for relaxation—he has trained himself to be able to fall asleep at a moment's notice—but to enjoy the companionship of his beloved wife, Alice, with whom his relationship is devoted and tender. They have no children, a matter of regret to both of them, though perhaps that very lack has resulted in a greater closeness between them. They share too a love of simple living and of the out-of-doors that finds expression in their trips to their cottage on Lake Winnepesaukee, New Hampshire. As a part of the Bald Peak Colony Club there are opportunities for swim-

ming, fishing, golf, and for tramping the woods and fields with dogs and gun in search of grouse, woodcock, or pheasants. Even in winter, if the doctor has a report to write or a deadline on an article to meet, they may drive up to the well insulated cottage for a happy and companionable weekend, far from the never-ceasing demands and responsibility of the clinic and of his position as Chief of Surgery at the New England Baptist Hospitals. Ordinarily he performs a thousand of the clinic's ten thousand annual operations. War duties cut into his time seriously enough to reduce that number by three or four hundred. Dr. Lahey is a busy and important man. He knows it, but he hasn't been spoiled by it.

Let an anecdote of the doctor's own choosing illustrate the point.

"When Mrs. Lahey and I were going to Honolulu on a vacation before World War II, the American College of Surgeons, ascertaining that I was going, asked me to inspect the Queen's Hospital as to whether or not it could be classified as Grade A qualification, which I agreed to do. I went to Queen's Hospital and saw the medical director, Dr. Niles Larson, looked the hospital over, looked the records over and approved thoroughly of it. Following this Dr. Larson said that there was a surgeon of German extraction in the operating room, operating on a patient for gallstones, and that I would probably be interested to go up and see him do it. Dr. Larson stated that he could not go with me but sent a nurse up with me. The nurse dressed me in a cap and gown, opened the door, I went in and she stayed out. The doctor who was operating had a number of visitors; he looked up and no one introduced me and so I introduced myself by saying, 'I am Dr. Lahey from Boston,' and the surgeon replied, 'Well, what of it?' It was an amusing and also a chastening incident."

Dr. Lahey's contributions to the progress of surgery have been varied and significant. Their worth is attested by the list of honors that have been bestowed upon him. He holds the Honorary Degree of Doctor of Science from Tufts College, from Boston University, from Northwestern University. In 1946 he was given the Medal for Merit by the Secretary of the Navy and the Certificate

of Merit by President Truman. From the American Gastroenterological Society he received the Friedenwald Medal, and from the Boston Surgical Society the Henry Jacob Bigelow Medal for accomplishments in surgery. It is that award that Dr. Lahey cherishes with special pride because it was given by his own confrères in his own town. Boston is not a town given to superlatives; Bostonians have an ingrained habit of weighing their words carefully. Therefore some of the remarks made upon the occasion of the presentation are well worth quoting.

The award is made for "new and valuable work in surgery or in fields connected with it." The medal was first awarded in 1921 to Dr. William J. Mayo. Since then eight other awards have been made, this present one being the tenth. (The other recipients were Drs. William W. Keen, Rudolph Matas, and Chevalier Jackson, Mr. George Grey Turner, and Drs. John M. T. Finney, Harvey Cushing, Edward W. Archibald, and Allen O. Whipple. Surgeons of the United States, England and Canada are represented.)

The Society has been chary about awarding the medal to one of its own members, and it can be accepted as fact that before doing so it has interpreted the terms of the award with more than usual stringency. In consequence, only one member has previously received the medal: Dr. Harvey Cushing.

Tonight it gladly honors another member. Dr. Frank H. Lahey, director of the Lahey Clinic here in Boston, on the basis of his accomplishments not only in the field of surgery but also in those broader fields that are connected with it well merits inclusion in this distinguished group of recipients. His mastery of thyroid surgery and surgery of the esophagus and bowel, for example, is but an indication of the scope of his technical skill.

The presidencies of the American Medical Association and the New England Surgical Society, the governorship of the American College of Surgeons and membership, both honorary and regular, in many other surgical societies point to his great influence among the medical profession. He has held professional posts in Harvard and Tufts College medical schools. The Lahey Clinic is famous for the opportunities it affords for graduate studies. Without his steadying influence during the war, the civilian physician situation would have been a serious menace to the public health. Even now, his influence is being continually exerted as a member

of the Presidential Advisory Committee on the Integration of Medical Services in the Government to the end that, among other things, the veterans shall receive better care.

Nor should we forget in honoring Dr. Lahey to do equal honor to Mrs. Lahey. All in this audience know what profound influence a surgeon's wife exerts on the surgeon. Without her sustaining aid his courage would many times falter; without her encouragement he would never be inspired to rise to heights believed by him to be beyond his reach. She puts up with long lonely hours, a frequently disrupted household and those temperamental peculiarities that are characteristic of a person who by nature and by training is above all things an individualist. Dr. Lahey will, I am sure, agree with me that without the devoted and loyal support given him by Mrs. Lahey he would never have achieved even a modicum of the deserved success that has been his.

Dr. Lahey—superlative surgeon, doctor who teaches doctors, redoubtable administrator, adviser of Presidents in war and peace and, above all, a man who has the courage to be honest with himself—as the representative of the Boston Surgical Society I take great personal pleasure in having the honor to present to you in its name the Henry Jacob Bigelow Gold Medal.

There is in Dr. Lahey's office another symbol of achievement of which he is justifiably proud. It is a simply lettered framed certificate designating Frank Howard Lahey as an honorary member of the Royal College of Surgeons in England. His pleasure in being so honored was reflected by his colleagues in London when he delivered a lecture there before the College.

They were fortunate to hear him too, for in addition to having something important to say, Dr. Lahey has the even rarer gift of being able to say it well. He speaks in public with a briskly confident manner, a use of concise and telling phrase, with clarity and directness. The same qualities are evident in the informal summaries he gives for the instruction of students who are invariably present and as a matter of courtesy to the visitors attending his operations. Indeed a steady monologue accompanies his every action so that each operation becomes a lecture and a demonstration. Infinitely patient, gentle, painstaking, Dr. Lahey cares little for speed, never loses his nerve, becomes even steadier and calmer in moments of crisis. These

are more frequent than one might think, since Dr. Lahey is often called upon to correct earlier mistakes made by others, to act as a court of last appeal.

UNDERLYING the smooth precision of technic is a coordinated team work of which Dr. Lahey and the clinic are properly proud. Each operating team is a carefully drilled, thoroughly experienced unit capable of working together with the utmost professional accuracy. Always there is acting as anesthetist a trained M.D. who watches pulse, heart-beat, cyanosis, respiration—who quite literally holds a watching brief for the patient. Each assisting nurse is well trained, able. Anticipating Dr. Lahey's every need is his silent, dependable, perceptive operating nurse, Blanche Wallace. She has been with the doctor for twenty-four years, knows by a sure instinct developed in that long association, what instrument to place in his reaching hand. He may, perhaps, request a better light, ask for his magnifying spectacles that enlarge organs undergoing scrutiny two and one-half times. Doubtless it is this almost magical efficiency of the operating amphitheatre that makes an occasional blunder so glaring. With its perpetrator Dr. Lahey is bleakly pitiless. "You cannot afford to *think* something is right. You must *know*."

Dr. Lahey knows because he has observed, experimented, learned, remembered. And the thousands of anxious but hopeful souls who crowd the Commonwealth Avenue clinic year after year demonstrate their faith in his knowledge. Some of them are wealthy and famous, though neither their names nor their diseases would ever be divulged by any member of the clinic staff. Many who crowd the small waiting rooms or diffidently answer the summons of a nurse are poor people—Boston's poor, New England's poor. Indeed, one-third of the total volume is charity work. Very probably the charity patients too may be examined by Dr. Lahey himself. Sometimes, however, they don't know it; one woman complained bitterly that she had been seen only by subordinates. In the slight, quiet, blue-eyed, sandy-complexioned man who still looks far younger than his sixty-seven years she had not recognized "the great Dr.

Lahey." Years ago there were even more serious penalties attached to his slender build and boyish appearance, for on one occasion a senior doctor declared that such a stripling was certainly too young to operate!

The convenient blanket title "head of the Lahey Clinic" covers a great many more duties than seeing patients and performing several hundred operations a year. Admittedly those functions serve the first aim of the institution, viz., to get people well, but Dr. Lahey visualizes other purposes, and all of them are materially advanced by his own activities. His design is fivefold:

- I. We must get people well.
 - II. In getting people well, we must investigate and develop new methods.
 - III. We must train men in the new technics in order to perpetuate and to spread what we have learned.
 - IV. We must serve as an informal postgraduate center.
 - V. We must write and we must talk—with certain reservations. For we must keep still when we have nothing to say, and we must never create openings in order to satisfy our ego or for mere publicity.
- Dr. Lahey has been particularly outstanding in investigating and developing new methods. Four operations have been named for him. His work in thyroid operations, together with the closely associated studies in metabolism and anesthesia, is world famous. His development of two-stage operations to lessen the shock of surgery to patients already dangerously weakened has been literally life-saving to hundreds. And he is constantly investigating, improving, discovering. One of the latest innovations in thyroid surgery is the pre-operative use of the thiouracil compounds which often makes two- or three-stage operations unnecessary, and which cut the average hospital stay to about six days. Dr. Lahey and his clinic doctors (with an impressive history of some 27,000 thyroid operations out of which they lost only 100 patients) have also found that thiouracil or propylthiouracil will bring down the basal metabolic rate almost exactly one point per day.

To make new procedures, particularly surgical technics, available for teaching purposes, Dr. Lahey

has colored films taken of certain operations, thus coordinating his activities as operating surgeon and as instructor.

IN ADDITION to the fifty-three full time staff members of the clinic, among whom are Dr. Richard Cattell in general surgery and Dr. Gilbert Horrax, worthy successor to Dr. Cushing in brain surgery, there are some ninety fellows working and being trained. Eleven of these are working under five staff specialists in a special school of anesthesia. From it there are sent out all over the country remarkably well qualified young men to act as heads of departments in hospitals, medical centers, and institutions. They are products of Dr. Lahey's belief that an operating surgeon's mind and nerves may best be freed to deal with whatever emergency may arise by his working in unison with a skillful, conscientious anesthetist who acts as the patient's representative. So important does the doctor consider his anesthetists that in the recent remodelling of the building they have been given a room of their own for their paper work. And in the still compact and crowded quarters available that is a very real distinction!

To a perfectionist like Dr. Lahey the dream forever outruns actual accomplishment, but his ideal of having the clinic serve as an informal postgraduate center is a matter of solid fact amply attested by authority as outstanding as the American Medical Association. Incidentally, the doctor served a term as the Association's president beginning in the troubled and uncertain days of June 1940. He also served as president of the Interstate Postgraduate Medical Association of North America and of the American Association for the Study of Goiter. Characteristically, in his inaugural address before the American Medical Association, Dr. Lahey scorned to quibble or compromise. He took a firm stand and expressed his beliefs boldly. Speaking of his opinion that at that time the country was already committed to forceful opposition to Hitler he said: "I myself like it [the United States' position]. We have dared the dictator. It is too late to appease him, and the word has no meaning in his language. We should arrive at a conviction concerning isolation. Is it right? It is my conviction

that it is not. I prefer destruction if it need be to survival in cowering terror. Give me positive commitment rather than compromising, unsatisfying safety."

The year 1940 marked a personal milestone for Dr. Lahey too—his sixtieth birthday. He was quite aware of some of its implications and in his quietly methodical way had a complete physical check-up before accepting the added responsibility of the presidency of the A.M.A. It was left to his staff and colleagues to celebrate the occasion in fitting fashion with an exceptionally successful surprise party at the Algonquin Club. Former fellows of the Lahey Clinic had assembled with their chief on the evening of May 30 for their regular alumni dinner. (June 1 is the actual birthday date.) On the floor below was an impressive gathering of the leaders in many fields of surgery and medicine. At dessert time they all came up, champagne glasses in hand, to offer toasts, sing congratulatory ditties, and admire the many-tiered birthday cake ornamented with such symbols of Dr. Lahey's hobbies as a miniature train, an airplane, and a pointer. Training his own hunting dogs and managing them in field trials had long been a favorite pastime. Twice he had won national championships in the amateur class, but like his hunting preserve in Alabama the dogs had to be abandoned in the heavy stress of wartime duties. Perhaps the patience was diverted from training dogs to teaching medical students! It is said that carving that elaborate confection was the one occasion on which Dr. Lahey was hesitant and timid with his knife! Certainly he was more visibly touched with emotion than ever in an operating room.

A more substantial memento derived from that sixtieth birthday party, viz., the Birthday Volume, a collection of studies by some sixty well-known doctors on their individual specialties or on matters influenced by Dr. Lahey. For example Dr. Cattell's piece on Lahey resection for cancer of the rectum, and Dr. Crile's discussion of the surgical treatment of essential hypertension. The book is fittingly dedicated:

We of the medical profession, partakers of that fame which you have gained for us no less than for yourself, offer to you this birthday volume, in which you find yourself reflected more often than we intend to confess. You have honored medicine,



A moment of relaxation for Dr. Lahey—and some of his prize-winning hunting dogs.

and medicine delights to honor you. This is our birthday gift to you, our friend, advisor, and inspiration.

Those who work for him report in less flowery terms on that quality of inspiring others. "There are lots of ways of getting people to do their best for you. If they're efficient—and the doctor takes care to make good and sure they are—one of the best ways to keep 'em that way is to let them strictly alone. He can do that, and yet you always know when you come into the clinic whether he's here or not. He drops the spark, makes others move. After talking to him, people get enthusiastic and start to generate ideas on their own." And then, more reflectively: "He's the kind of man who, by the force and drive of his very nature would have accumulated money and prestige if he'd started out lacking it—which he didn't."

"He's fair too, hears your side promptly. His door's always open. The patients too learn very quickly that he's one of the easiest men at the clinic to see. That's because he sees everyone *now*; does everything *now*; he never postpones things or

lets them pile up on his desk. And yet he probably gets through more work than anyone else. When he makes up his mind—and he makes it up quick too for he says he has a 50 per cent chance of being wrong—he acts fast and nothing stops him."

Along with his more forceful traits Dr. Lahey has a keen eye for detail. As one might guess from his own meticulous neatness, he dislikes sloppiness of all varieties among his associates and employees, whether evident in an unruly long bob, a couple of extra pounds around the hips, or unpolished dusty shoes. Concerning the latter he sent around a notice, accompanying it with cans of three shades of polish strategically disposed about the clinic.

Patients are held to the same austere standards. A placard in the entrance hall states clearly: "No smoking in the vestibule. There is a receptacle on the street corner for your cigarettes." And the memory of the hard straight chairs in the always crowded waiting rooms is ineradicable for anyone who has gone through the clinic. Those chairs, along with the absence of magazines to read, are an indication of Dr. Lahey's belief that sick people

like to talk to other sick people about their ailments. The doctor's courtesy is brisk and business-like, but it is unfailing. And its essential human understanding is mirrored in the precepts inculcated into every clinic employee from receptionist to examining doctor. "Remember," says the chief, "the people who come here are sick—they deserve and should have special kindness."

He's a good business man too. Always has the money in the bank before he builds, and then, liking the close association of a manageable group, jealously guards against overexpansion. He is capable of shrewd appraisal of Boston real estate values, a knowledge he gladly shares with any young clinic fellow faced with the necessity of providing living quarters for his family. Dr. Lahey's own home is but a few steps from the clinic, round the corner on Bay State Road. Thus he is spared any problem of commuting, and can literally use every moment to good advantage. His regimen, though frequently broken by speaking tours and lectures, is strict. The doctor is up by six, breakfasts with his wife at seven fifteen. At eight he starts operating, either at the Deaconess or New England Baptist Hospital. The clinic lacks operating facilities of its own. He lunches quietly at home, always finding a quarter or half hour for a relaxing nap. In the afternoon he sees patients and attends to other duties at the clinic until six. He dines at seven, and even should he be at a social function he is very apt to slip away for his usual ten o'clock bedtime. He neither smokes nor drinks—not that he holds convictions on the subject; merely that it is easier not to. A rigid routine, but one that keeps him fit for his strenuous life.

AND so he goes about his manifold yet closely coordinated activities—a skillful and outstanding surgeon, but a great deal more than that; an originator of technics of operating and of bringing specialized, understanding medical care to thousands; an educator and directing force in medical training.

In the anniversary volume entitled *A History of the American Medical Association* celebrating a hundred years of service to the profession, Morris Fishbein evaluates phases of his contribution thus:

"His chief literary contribution, in addition to many periodical articles, is the Lahey Clinic number of the *Surgical Clinics of North America*. [Annually he gets out the June issue.] He is a member of the editorial boards of *Surgery, Gynecology and Obstetrics*, and of the *New England Journal of Medicine*.

"His particular contribution to postgraduate education has been in the form of well-prepared lectures, always illustrated with slides and movies, delivered before medical societies, regional clinics, seminars, institutes and medical schools. He uses but few notes, and speaks entirely from his own experience, and the results obtained at the Lahey Clinic."

That estimate is inclusive and doubtless just, but it leaves out the warmth and sincerity of feeling felt for Dr. Lahey by those who have known him well, worked closely with him. Dr. Arthur Booth, past chairman of the Board of Trustees of the A.M.A., speaks for many when he says:

"That he has so many fond friends and enjoys such a broad acquaintance among doctors is due to his delightful personality, his approachableness and a willingness to give generously of his time and energy to his fellows. He has always found it difficult to decline an invitation to present scientific papers before medical societies or to serve in official capacities in medical organizations.

"I am particularly impressed that he accepts with such enthusiasm the broader responsibilities of his profession. To work within the close range of the doctor-patient relationship is obviously most essential and commendable, and by far too many very excellent men essay no further. Fortunately, it is given to some to look beyond the narrow confines of the consultation room or the clinic to that broader horizon where loom the vital problems of the advancement of medical science and art, especially in the field of supervision and direction of the Medical School and Hospital."

And a colleague who worked beside him in the tense war years sums it up even more tellingly.

"Dr. Lahey has said frequently, that 'he is devoting his life to the training of young physicians for better service in medicine and surgery,' and therein will be his noblest monument."

L. C. DEINARD



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EDITORIALS

AMERICAN SPECIALTY BOARD CERTIFICATION

IT is quite consistent with the straightforward and somewhat aggressive policies of this relatively new journal, to discuss this subject and the controversy that is now brewing around it.

Specialty Board certification was seriously begun only about twenty years ago. Since that time, sixteen American Boards have established themselves as a profound influence on American medicine and its trends. All of these Boards started and have continued with two main avowed purposes, namely, to improve the standards of the practice of medicine in the various specialties, and to provide standards by which men qualified by actual training, experience, and ability, could be recognized as specialists.

There can be no question but that the Boards have been organized and conducted on a high plane; that medical politics have not entered into their functioning; that personal aggrandizement on the part of the Directors of the Boards cannot be charged in any degree; and that the leaders of the profession now conducting the affairs of the Boards are determined to keep them "clean." These men are entirely representative of the profession because they are appointed by the special national societies and academies which they represent, including the American College of Surgeons and the special sections of the American Medical Association. Their actions and rulings have been judicial and fair; in fact, no charge of unfairness toward candidates has ever been leveled at any Board. Nevertheless, the medical profession at large is becoming more and more critical of the Amer-

ican Boards and their certifications.

The Boards have been charged with setting up a "medical aristocracy" of specialists with which the general practitioner and the uncertified specialist are at a disadvantage. That this "aristocracy" has no barriers of race or color, its only card of admission being that of demonstrated ability, does not lessen the criticism.

It is charged that specialization and certification have been so overemphasized that all young doctors now aim to be specialists and too few want to be general practitioners, to the detriment of the public.

Discrimination has been alleged on the ground that many hospitals now require that anyone permitted to perform surgical work within them must be certified by an American Board, thus excluding the general practitioner who wants to do his own surgery. Going further, some hospitals have required that all staff appointments be restricted to American Board Diplomates. Another charge has been that older, though qualified, men who have not sought certification are being removed from their hospital staff positions and replaced by young men recently out of residencies but certified.

Some of these complaints have truth in them, others have only enough basis in fact to provide a complaint as an argument. Much of the criticism directed at the Boards has been unmerited.

In the first place, the Boards have accomplished for American medicine and the American public precisely what they set out to do. The standards of practice of medicine in this country have been vastly improved. The active educational program in the greatly expanded residency training system in American hospitals has bettered the training and practice of every

doctor exposed to it in a "residency approved" hospital, from interns up to and including the chiefs of staff. This is so regardless of whether they were working for some Board's certification, training for general practice, or in charge of and supervising the educational program. Everyone has profited, the patients most of all.

The Boards have succeeded in their aim to establish minimum standards of qualification, experience, and ability for men desiring to be recognized as specialists. It is no longer possible for a man to go away from home "for a postgraduate course" here or abroad and presently reappear as a full-fledged and unquestioned specialist.

No wonder some hospitals grasped at the chance to eliminate, by requiring certification for "courtesy privileges," some of those who "want to do their own surgery" regardless of lack of ability. What right has an untrained or poorly trained man to subject a patient to his surgery?

But the hospitals were wrong in making rulings requiring certification for staff appointments. The Boards disclaim any responsibility for such regulations, because they refute the fundamental principle of the Boards that Dispensary, Assistant, and Associate Staff hospital appointments provide an excellent training and proving-ground for young men. Many of these men might have been only partially trained by the residency system and logically seek to complete their Board's required credits by the preceptorship method under Assistant Staff appointments.

Senior Staff regulations having a reasonable degree of elasticity meet all criticisms. A simple rule in the "By-laws" of this writer's hospital staff should be quoted and more generally adopted to allow for the recognition and retention of acceptable, qualified men who have not been and never will be certified. "Members of the Senior Staff shall be required to be recognized specialists, and must be Diplomates of their respective specialty Boards, *except for outstanding reasons recognized by a three-quarter's vote of the Senior Medical Staff.*" Such a rule as this provides adequately for the gen-

eral practitioner in the Department of Medicine, even on the Senior Staff, and certainly on the Associate or Assistant Staffs, where there should be ample place for general practitioners of ability. Even when hospitals, generally, establish formal Departments of General Practice this present regulation will need no alteration, because it is already so comprehensive.

Neither the general practitioner nor any other has valid reason to be antagonistic to these honest efforts toward improvement of the practice of medicine. Certification by a specialty Board is not another form of discrimination against anyone, nor is it the sole means of determining ability. It is, however, a thoroughly reliable yardstick by which the claim of specialist can now be measured.

P. T.

MEDICAL ASPECTS OF ANXIETY

IT is well accepted by all of us that there is no sharp dividing line between the normal person and one who has an emotional illness. In all of us our adjustment varies from day to day. No one of us is ever a perfect success or a perfect failure. In many ways our adjustment can be symbolized by a pendulum which can be swayed from side to side by various factors or forces acting on it, but which returns to a central resting state when the force is removed. Some of us are thrown off balance more easily; others of us require greater stresses to disturb our equilibrium.

The tendency toward emotional illness is a *quantitative* thing: in some the tendency is small and the stress has to be great; in others where the tendency is greater, the stress can be less. All of us are constantly adjusting to conflicts and stress, and there is almost never a single cause in any emotional illness. At least four factors are always important in understanding any maladjustment; these factors are the previous experience of the individual, his own personality structure, his personality needs, and the environmental demands.

In such a complex and changing adjustment, it would not be unusual for inner conflicts to generate a feeling of inner tension which we sense consciously as anxiety. Indeed, it has been said that anxiety is the universal disease of our time, and that psychosomatic disease is the visceral expression of our anxiety. This view that anxiety is the predominant reaction in a functional illness is a valuable and unifying concept. In the various psychosomatic disorders, the symptom is due to a chronic and exaggerated state of the normal physiology of the emotion, with the feeling part repressed. Furthermore, chronic anxiety may produce long-continued visceral dysfunction which may in turn eventuate in structural changes of an organ.

We have now begun to formulate certain types of illnesses in which emotional factors play an important role. However, it is true that anxiety may affect any somatic function. Some of the more common manifestations of it are:

1. Gastrointestinal reactions.

Peptic ulcer-like reaction, chronic gastritis, mucous colitis, hyperacidity, pylorospasm, etc.

2. Cardiovascular reactions.

Paroxysmal tachycardia, pseudoangina pectoris, some types of hypertension, and neurocirculatory asthenia.

3. Genitourinary reactions.

Dysuria, impotence, frigidity, some menstrual disturbances, etc.

4. Skin reactions.

Some allergic responses (angioneurotic edema), factitia dermatitis, factor in certain eczematoid conditions.

5. Respiratory reactions.

Asthma, nasal mucosal congestion, etc.

Man, thus, is an integrating organism maintaining a balance between the external and internal forces which determine his activities. When this balance is disturbed, disordered personality functioning and disordered body functioning results. Psychosomatic reactions are only the somatization of anxiety.

F. G. E.

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New Drugs

Information published in this department has been supplied by the manufacturers of the products described.

PENICILLIN POTASSIUM TROCHES

PURPOSE: For intensive, topical penicillin therapy.

DESCRIPTION: Each troche contains penicillin 10,000 units, in a slowly dissolving, pleasantly-flavored base.

INDICATIONS FOR USE: Vincent's stomatitis, streptococcus pharyngitis, and tonsillitis.

DOSAGE AND ADMINISTRATION: Penicillin troches should be placed anywhere in the mouth, preferably into the buccogingival sulcus, and allowed to dissolve without chewing. One troche should be taken every one to four hours (depending on the severity of the infection) and just before retiring. If the patient awakens during the night another troche should be taken. With clinical improvement, dosage may be gradually reduced. As a general rule penicillin treatment is maintained until after the patient has been asymptomatic for at least forty-eight hours.

CAUTIONS: Topical use of penicillin may cause a contact dermatitis (urticaria, swelling, etc.) in hypersensitive individuals. In the mouth, hypersensitivity may be manifested by itching and swelling of the mucous membrane. With the occurrence of side effects the use of penicillin should preferably be discontinued. If continued administration is deemed necessary, the dose should be reduced to a minimum and great caution employed.

HOW SUPPLIED: Penicillin troches, 10,000 units, vials of 12 troches, boxes of 4 vials.

PRODUCER: Winthrop-Stearns, Inc., New York 13, N.Y.

DOLOPHINE

PURPOSE: Analgesic for relief of pain.

COMPOSITION: Heptanone derivative (4,4-diphenyl-6-dimethylamino-heptanone-3 hydrochloride) and an entirely different type of compound from either morphine or isonipecaine.

DESCRIPTION: A white crystalline substance, soluble in water and alcohol but insoluble in ether. It has a bitter taste and melts at 236° to 236.5° C.

INDICATIONS FOR USE: For control of pain and discomfort following surgery. Also used for alleviation of pain caused by ureteral stone; controlling pain due to metastatic lesions of malignant tumors and during treatment of pleuritic pains of pulmonary tuberculosis.

CAUTIONS: Nausea, vomiting, lightheadedness, drowsiness, dryness of the mouth, diaphoresis, and mental depression have occurred, but were not severe enough to necessitate stoppage of the drug. Not recommended for use alone as preanesthetic medication. Dolophine must be considered a potentially addicting drug and must be administered with caution similar to that attending the use of morphine until its status in general practice is established.

DOSAGE AND ADMINISTRATION: For moderate pain, 2.5 mg. of Dolophine given orally usually are effective for three to four hours. Severe pain may be controlled by oral dosage of 5 to 10 mg. Subcutaneous administration is not painful,

and a somewhat more marked effect is obtained by hypodermic medication.

HOW SUPPLIED: Tablets Dolophine, 2.5 mg., 5 mg., and 7.5 mg., in bottles of 100 and 1,000. Ampules Dolophine, 10 mg. per cc., in individual 20-cc. rubber stoppered ampules. Syrup Dolophine, 10 mg. per 30 cc., in bottles of one pint and one gallon.

PRODUCER: Eli Lilly and Company, Indianapolis 6, Ind.

TABLETS ALUPEC

PURPOSE: Formula for quick and sustained antacid action.

COMPOSITION: Each tablet represents:

Aluminum hydroxide dried gel.....	10 gr.
Pectin.....	2½ gr.
Magnesium carbonate.....	1¼ gr.
Saccharin and aromatics.....	q.s.

One Alupec tablet will neutralize not less than 165 cc. of N/10 hydrochloric acid.

INDICATIONS FOR USE: Treatment of hyperacidity, including that accompanying peptic ulcer, as an aid to the promotion of healing and to control minor hemorrhage and relieve pain.

DOSAGE AND ADMINISTRATION: Adult, 1 tablet one-half to one hour after meals, repeated after two to four hours if indicated. Allow to disintegrate slowly in mouth, or crush or chew; follow with water or milk. When prescribed as an adjunct to ulcer treatment, dosage should be regulated by the physician.

HOW SUPPLIED: In bottles of 60 (6 to the box) and bottles of 500. Also available in liquid form.

PRODUCER: Pitman-Moore Company, Indianapolis 6, Ind.

URESTRIN

PURPOSE: For relief of menopausal symptoms.

COMPOSITION: The crystalline natural estrogens in this aqueous suspension are comprised of approximately 95 per cent estrone and 5 per cent estradiol, hippulin, and equilin. Prepared from estrogens obtained from urine of pregnant mares. Each cc. contains:

Estrogenic substances.....	2 mg.
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(20,000 International Units)

Physiological salt solution.....q.s.

INDICATIONS FOR USE: For intramuscular use only, for administering estrogens suspended in water for relief of menopausal symptoms and for prolonging the period of relief.

DOSAGE AND ADMINISTRATION: The intramuscular injection of 2 to 4 mg. at intervals of one week will usually suffice, but more refractory cases may require more frequent administration.

HOW SUPPLIED: In 1 cc. vials.

PRODUCER: The Upjohn Company, Kalamazoo 99, Mich.

ABBOTT'S LIVER INJECTION, U.S.P.

PURPOSE: A parenteral solution of liver for intramuscular administration.

DESCRIPTION: Prepared from fresh liver by a uniform method designed to retain maximum amounts of the anti-anemia principle. It contains in concentrated form the Cohn liver fraction G. It is low in total solid content and high in hematopoietic activity. Injections are relatively non-irritating.

INDICATIONS FOR USE: Indicated for the treatment of the average uncomplicated case of pernicious anemia in relapse and for the maintenance of a normal blood picture.

DOSAGE AND ADMINISTRATION: Injection should be made intramuscularly. Least discomfort is experienced when the injection is made deep into the upper, outer quadrant of the gluteal muscle. Dosage requirements vary considerably according to the severity of the case. Each unit of Abbott's Liver Injection, U.S.P., represents the quantity of anti-pernicious anemia principle that will produce the clinical and hematopoietic responses defined as 1 U.S.P. unit (injectable) when given daily under controlled conditions to qualified patients with addisonian pernicious anemia.

HOW SUPPLIED: In three strengths: 15 units per cc., in 1-cc. ampules and 10-cc. vials; 10 units per cc., in 1½-cc. ampules, 10-cc. vials, and 30-cc. bottles; and 5 units per cc., in 10-cc. vials and 50-cc. bottles.

PRODUCER: Abbott Laboratories, North Chicago, Ill.

OBEX MULTIVITAMINS

PURPOSE: Treatment of general nutritional deficiencies.

COMPOSITION: Each capsule contains:

Bone meal Po. Purif.	260 mgm.
Dibasic calcium phosphate	130 mgm.
Ferrous gluconate	65 mgm.
Vitamin A	5,000 I.U.
Vitamin D	1,000 I.U.
Thiamin HCl	5 mgm.
Riboflavin	3 mgm.
Pyridoxine HCl	2 mgm.
Calcium pantothenate	2 mgm.
Niacinamide	25 mgm.
Ascorbic acid	50 mgm.
Tocopherol (Equiv.)	3 mgm.
Inositol	10 mgm.
Folic acid	0.5 mgm.

INDICATIONS FOR USE: Prophylaxis therapy for expectant and nursing mothers; also, where general nutritional deficiencies exist in child and adult.

DOSAGE: 1 to 3 capsules daily as suggested by the physician.

HOW SUPPLIED: Bottles of 100 and 1,000 capsules.

PRODUCER: Ingram Laboratories, Inc., San Francisco, Cal.

TOMECTIN

PURPOSE: A palatable, nontoxic preparation designed for treatment of diarrhea of nonspecific origin as well as bacillary dysentery.

COMPOSITION: Each gm. contains:

Nickel pectinate	150 mg.
Sodium chloride	50 mg.

Together with all factors naturally present in

dried fresh tomato pulp. 800 mg.
DOSAGE AND ADMINISTRATION: Children and adults: 1 to 2 heaping tablespoonfuls (6 to 12 gm.) in water every two to three hours or after each bowel movement until recovery. Infants: 1 to 3 heaping teaspoonfuls every three hours or at each feeding.

HOW SUPPLIED: In wide-mouthed bottles each containing 50 gm.

PRODUCER: Ayerst, McKenna & Harrison, New York 16, N. Y.

DEXEDRINE SULFATE ELIXIR

PURPOSE: Central nervous stimulant.

COMPOSITION: The liquid dosage form of Dexedrine, each 5 cc. (1 teaspoonful) supplies the same amount of Dexedrine Sulfate (dextro-amphetamine sulfate, S.K.F.) as the standard 5 mg. tablet.

DESCRIPTION: The Elixir is the dosage form of choice in instances when it is desirable to produce the therapeutic effect of Dexedrine with greater speed than tablet medication allows.

INDICATIONS FOR USE: In depressive states, Dexedrine restores the patient's sense of well-being and capacity for work. The speed of action dispels as quickly as possible the characteristic "morning fatigue." In obesity, Dexedrine is established as the most effective drug for curbing appetite. It is also valuable in narcolepsy, postencephalic parkinsonism, and alcoholism.

CAUTIONS: Contraindicated in agitated prepsychotic states, hyperexcitability, hypersensitivity to sympathomimetic compounds, and those cases of coronary or cardiovascular disease in which vasoconstrictors are contraindicated. Should be used with caution in cases with marked hypertension.

DOSAGE AND ADMINISTRATION: Depressive states—5 mg. to 10 mg. daily, one-half of the dose on arising, and the other half before noon. For control of appetite—15 mg. to 20 mg. daily, in 3 equal doses—before breakfast, at 11 A.M., and at 4 P.M.; or give largest dose at time of greatest hunger. Alcoholism—5 mg. to 15 mg. daily, one-half dose on arising, the other half before noon. Narcolepsy—10 mg. to 25 mg. daily, one-half of the dose on arising, the other half before noon.

HOW SUPPLIED: In 6 fluidounce bottles.

PRODUCER: Smith, Kline & French Laboratories, Philadelphia 5, Pa.

TIMOFAX

PURPOSE: Undecylenate ointment for the treatment of "athlete's foot."

COMPOSITION: Timofax contains undecylenic acid 10 per cent, as free acid and potassium undecylenate, in a scented, vanishing cream base.

INDICATIONS FOR USE: In acute and subacute dermatophytosis pedis ("athlete's foot"). In refractory, chronic cases, particularly those with established sensitivity to drastic chemical agents, a rest period followed by Timofax therapy may prove valuable.

HOW SUPPLIED: In ¼ ounce collapsible tubes.

PRODUCER: Burroughs Wellcome & Co., New York 17, N. Y.

PANSULFA

PURPOSE: Triple sulfonamide suspension for use in sulfonamide therapy.

COMPOSITION: Each 5 cc. teaspoonful contains 0.5 gm. ($7\frac{1}{2}$ gr.) combined sulfonamides.

DESCRIPTION: Liquid combining microcrystalline sulfathiazole, sulfadiazine, and sulfamerazine in 1:1:1 ratio.

INDICATIONS FOR USE: Pneumococcic, streptococcic, meningococcic, and staphylococcic infections, scarlet fever, rheumatic fever, erysipelas, otitis media, tonsillitis, urinary infections due to *E. coli*, *Staphylococcus albus*, *Proteus* and *Pseudomonas*.

DOSAGE: Adults—an initial dose of 8 teaspoonsful, followed by 2 teaspoonsful every 4 to 6 hours. Children—one teaspoonful for each 5 pounds of body weight per day, given in divided doses at four-hour intervals.

HOW SUPPLIED: 12-ounce bottles.

PRODUCER: The Wm. S. Merrell Company, Cincinnati, O.

FOLIX-B

PURPOSE: For treatment of anemia.

COMPOSITION:

Folic acid	3.3 mg.
Ferrous gluconate	300.0 mg.
Thiamin hydrochloride	3.0 mg.
Riboflavin	6.0 mg.
Niacinamide	30.0 mg.
Pyridoxine hydrochloride	0.1 mg.
Calcium pantothenate	1.0 mg.

DESCRIPTION: A new hematopoietic formula combining folic acid with iron and B vitamins.

DOSAGE: One tablet three times a day.

CAUTIONS: In pernicious anemia with neurologic signs, liver should be given.

HOW SUPPLIED: Bottles of 25 and 100 tablets.

PRODUCER: Cutter Laboratories, Berkeley 1, Cal.

CHLORGUANIDE HYDROCHLORIDE TABLETS

PURPOSE: Prophylaxis of malaria.

COMPOSITION: Chlorguanide is the shorter, nonproprietary name assigned by the Malaria Study Section of the National Institute of Health to N_2 -*p*-chlorophenyl- N_2 -isopropylbiguanide. The hydrochloride of chlorguanide is a stable, white, crystalline powder, bitter-tasting and odorless, with a melting point of 240° C.

DESCRIPTION: Chlorguanide exerts a twofold effect as an antimalarial drug. It has a powerful action on the parasites in the red blood corpuscles, and it is one of the few antimalarial drugs that attack exoerythrocytic forms, and the only one that is active against these forms in more than one species. The potent action of the drug precludes the necessity of giving large doses. It does not stain the skin. It attacks both exoerythrocytic forms and blood forms of the malarial parasite. The gametocytes are attacked indirectly.

CAUTIONS: Occasionally nausea and vomiting have occurred from one-half to one hour after administration, but these minor symptoms were attributed to the disease rather than to the drug, and ceased with improvement of the clinical condition.

INDICATIONS FOR USE: In the treatment of both benign and malignant tertian malaria, chlorguanide inhibits development of the schizonts, and results in degeneration of asexual parasites before the formation of mature schizonts. Effective in clinical cure, radical cure, causal prophylaxis, and suppressive therapy in benign tertian malaria and malignant tertian malaria.

DOSAGE AND ADMINISTRATION:

Clinical cure of malignant or benign tertian malaria (suppression of acute attack)	0.1 gm. (1 tablet) 3 times daily for ten days
Radical cure of malignant tertian malaria	0.1 gm. 3 times daily for ten days, 0.1 gm. twice daily for fourteen days, or 0.2 or 0.3 gm. twice daily with a corresponding reduction of the treatment period
Radical cure of benign tertian malaria	0.1 gm. once a week, after the acute attack has been controlled
Causal prophylaxis of malignant tertian malaria	0.1 gm. (1 tablet) twice a week
Suppressive therapy of benign tertian malaria	0.1 gm. (1 tablet) twice a week or 0.3 gm. (3 tablets) once weekly

HOW SUPPLIED: In bottles of 100 and 1,000.

PRODUCER: Sharp & Dohme, Philadelphia 1, Pa.

ELIXIR LI-BETARON WITH FOLIC ACID

PURPOSE: For treatment of hypochromic anemia and as maintenance therapy in certain types of macrocytic or normocytic anemias.

COMPOSITION: Each 30 cc. (1 fluidounce) represents:

Ferrous gluconate (equivalent in elementary iron to 262 mg. per fluidounce)	2.27 gm. (35 gr.)
Folic acid	5 mg.
Thiamine hydrochloride	18 mg.
Riboflavin	6 mg.
Nicotinamide	60 mg.
Pyridoxine hydrochloride	2 mg.
Calcium pantothenate	5 mg.
Whole liver (as liver concentrate 1:20)	56.7 gm. (2 ounces)

(Total soluble constituents of 2 pounds of whole liver per pint of Li-Betaron with Folic Acid Elixir.) Also choline and other factors natural to liver.

DOSAGE AND ADMINISTRATION: Adults: A tablespoonful followed by water twice daily after meals. Children (6 to 12 yrs.): A teaspoonful followed by water three times daily after meals. Children (1 to 6 yrs.): A teaspoonful followed by water twice daily after meals. Infants (under 1 yr.): 20 drops from a standard dropper (10 minims) in milk four times daily.

HOW SUPPLIED: 8 fluidounce and one-half gallon bottles.

PRODUCER: Warren-Teed Products Co., Columbus 8, O.

Medicine Makes News

CUTTER LABORATORIES RESUME SHIPMENTS

ANNOUNCEMENT that Cutter Laboratories, Berkeley, California, are ready to resume shipment of Cutter solutions in Safitflasks from its Berkeley and branch warehouses has been made by Fred A. Cutter, Vice President of the organization.

The full text of Mr. Cutter's statement is as follows: "We are now ready to resume shipment of Cutter solution in Safitflasks from our Berkeley and branch warehouses.

"We wish we could tell you that the cause of the contamination is now definitely known. We cannot truthfully do so. In the six weeks since we recalled our solutions, hundreds of thousands of flasks have been critically examined. Every piece of equipment and every instrument were meticulously checked. There was no evidence of equipment or instrument failure, and we could not definitely confirm closure failure or any other cause.

"We can assure you, however, that not a single bottle which was clear on visual inspection has been found to be contaminated, and that we will continue to do everything in our power to assure the safety that has been the cornerstone of our existence and growth for over fifty years."

A.P.M.A. MEDICAL SECTION BOARD ANNOUNCED

DR. THEODORE KLUMPP, President of the American Pharmaceutical Manufacturers' Association, has announced that the following ten physicians will serve as the Board of its recently created medical section:

Dr. Charles E. Dutches, Schenley Laboratories, Inc. (Chairman); Dr. J. B. Rice, Winthrop-Stearns, Inc.; Dr. Stanton M. Hardy, Lederle Laboratories Division, American Cyanamid Co.; Dr. D. K. Kitchen, Bristol Laboratories; Dr. Paul C. Barton, Brewer & Company, Inc.; Dr. R. L. Conklin, Ames Company, Inc.; Dr. George Hazel, Abbott Laboratories; Dr. Irwin C. Winter, G. D. Searle & Company; Dr. Paul Spickard, Rexall Drug Company; and Dr. John M. Shaul, Maltbie Chemical Company.

SYMPOSIUM ON STEROID HORMONES

FINAL plans for the Symposium on Steroid Hormones to be held at the University of Wisconsin from September 6 through 8, 1948, have been announced by Dr. Edgar S. Gordon, Chairman of the Symposium Committee and Associate Professor of Medicine at the Medical School of the University of Wisconsin. This symposium is a part of the Centennial celebration of the Wisconsin State University. The final program includes the chemistry, metabolism, and biological effects of the steroid hormones, and the clinical applications of these substances will be discussed in detail.

This meeting is presented under the direction of the University of Wisconsin and the National Research Council Committee on Growth acting for the American Cancer Society. The Wisconsin Medical School, McArdle Memorial Laboratory for Cancer Research, and the Department of Biochemistry of the University have organized the program.

NEW GRANTS FOR VITAMIN STUDIES

New grants-in-aid, totalling \$16,000, were awarded July 1 to scientists at four universities for vitamin research, according to an announcement by Robert S. Goodhart, M.D., Scientific Director, The National Vitamin Foundation.

The new investigations involve eye health, the nutritional status of school children, the relationship between pyridoxine (vitamin B₆) and fat metabolism, and the effects of time elements on the utilization of water-soluble vitamins. The new grants bring to \$126,320 the amount appropriated by the Foundation for nutrition research since March 1946.

Universities receiving the grants are Western Reserve University, School of Medicine, Cleveland, Ohio; University of Vermont, College of Medicine, Burlington, Vermont; Massachusetts Institute of Technology, Cambridge, Massachusetts; and the University of Southern California Medical School, Los Angeles, California.

Leaves from a Doctor's Diary

By MAURICE CHIDECKEL

July 1 . . . In his clinic today, gynecologist Allen was recounting the causes and cures of amenorrhea. For his clinical material he had Patricia Perkins who had not menstruated for three months. What didn't he mention? Ovarian dysfunction, atrophy of the endometrium, hypoplasia of the uterus, anorexia nervosa, disorders of metabolism, no estrin in the urine, and more and more causative factors. "This fine child of eighteen," he pointed to smiling Patricia, "is not married. Hence pregnancy is unthinkable." Utterly impossible. Who ever heard of an unmarried woman becoming pregnant? How could she? But "this fine child" called me this morning to tell that she has three hundred dollars cash. Would I please send her to a first class abortionist. How come?

* * *

July 2 . . . Several weeks ago Montgomery Boswell married for the second time. The bride told me that life without him would be an empty existence. Today I sent him to the hospital, as a dire emergency. "Madame," I told the wife, "your husband is not suffering from nervousness, and he does not need an operation, as you were told. He suffers from the bite of the female or widow spider, whose poison is fifteen times as strong as the poison of a rattlesnake. His life is to be despaired of. I fear he'll die." Her sister giggled. "When a female bites, she bites." Her bearded father shook his head approvingly. He turned to his married daughter. "Did he make you beneficiary of his policy?" he inquired with some anxiety. "Yes," said the wife. "Big policy?" father asked. "Forty thousand." Said the father, "Good." Said the sister: "Thank God. Come, I am hungry." And as all three

walked off to lunch, the wife remarked: "I really would like him to live a little longer." What a noble soul. How devoted.

* * *

July 3 . . . So it is said: The reason a dog has many friends is because the animal wags its tail, instead of its tongue. Even excruciating pain, danger, and tragic events cannot stop this wagging that is sometimes destructive. And the Wise Man saith, life and death are within the power of the tongue. There sat in my office Mrs. Ayrest, suffering from causalgia, that painful state that arises from a focus of nerve irritability resulting from nerve damage. She is to enter the hospital for a sympathectomy. Her pain apparently ceased with the entrance of big Ralph Corrigan. "Shame on you," were the first words that greeted him. "I passed by your house yesterday afternoon. Disgraceful. If you must make love to your wife in that shameful way, why don't you at least pull down the blinds?"

Corrigan at first laughed. "The joke is on you, Mrs. Ayrest. Yesterday, I was not even home. I was out of town." Suddenly he awakened to consciousness, looked bewildered, then, in my consultation room he broke down and wept. I succeeded in prevailing upon Corrigan to believe me that she mistook him for another man. She did not.

* * *

July 6 . . . Instructor of philosophy Sinwell Claude is alert, eccentric and of vile temper. In addition to his other "gifts" he mistreats his French wife, beats cruelly his adopted son of ten, and proclaims aloud to his students the doctrine of white supremacy. He is plagued by a peptic ulcer, and I fail to see why he

comes to consult me. His knowledge of psychosomatic medicine is something to marvel at. Each time he comes and he comes quite often, he never fails to discuss the correlation between frustrated desires and ulcer manifestations, the parasitic dependent desires arising from overindulgence in childhood and the development of symptoms when infantile cravings were denied. Today he entered smilingly. "I need your cooperation," he began. "No, not about my ulcer. I am organizing a national society. Not about the Negro. It's to be a society that will make all white men happy, and you are to be the national secretary of the American Society of Hedonism, the philosophy which makes pleasure the goal of life. The Greeks were right. The chief good of life is the enjoyment of personal pleasure in the gratification of desires. If it is our pleasure to eliminate a certain section of the population we shall do it. I think it's best that we call it by the modern name, Utilitarianism, which means to bring about the maximum pleasure of mankind. Are you with me? This organization will be our message to the ages." While he talked, he fingered a book of poetry that lay on my desk. I saw him tear out a page, and as he began to mutilate it I tore the end out of his hands.

It was probably William Cowper's "The Negro's Complaint." I only saved the last four lines:

Fleecy locks and black complexion

*Cannot forfeit Nature's claim;
Skins may differ, but affection
Dwells in white and black the same.*

He fled when he saw Edna Buck coming in. Edna is a lady of the evening, and she comes weekly for a checkup. Her followers must be protected. Edna is no general practitioner. She specializes in married men. "He is one of my best customers," she meant the philosophy instructor. "It is not nice of you to betray confidence," I remonstrated with her. She laughed. "Don't these



Present Methods in the Treatment of Infantile Paralysis

WALLACE H. COLE*

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL, MINNEAPOLIS

IN ORDER to discuss the present methods in the treatment of infantile paralysis, it is necessary first to review, to a certain extent at least, something of the symptomatology and course of the disease in general and to explain why an orthopedic surgeon has been asked to speak on this subject.

The literature on poliomyelitis is so voluminous that it is with definite hesitation that one adds another discussion to the long list of titles comprising the bibliography of the disease, and many already published papers could be read here with greater benefit than anything I can offer. However, reiteration of the basic knowledge which we have, incomplete as it is, and a summary of the more accepted means of treatment can do no harm and may even be of some slight value. Until a specific agent has been developed against the virus of infantile paralysis, no standardized method of treatment is possible in the acute stages, and the symptoms only can be combated. What appear to be the best methods in this fight will be discussed briefly here.

*Professor and Director of Division of Orthopedic Surgery, University of Minnesota Medical School, Minneapolis.

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In 1741 Andry, of the Faculty of Medicine of Paris, published a two-volume book in the preface of which he stated that "I have formed from the two Greek words, *Orthos*, which means straight, free from deformity, conforming to rectitude, and *Paidion*, meaning child, the word d'Orthopedie to express in one term the subject by which I propose to teach the various means of preventing and correcting in children the deformities of the body." At its very inception, therefore, the word *orthopedics* was coined to mean, as the subtitle of Andry's book states, "the art of preventing and correcting deformity." Since then the word has been adopted by that branch of surgery which is particularly interested in the mechanical framework of the human body together with the knowledge of the function and structure of the body which that implies. This specialty has expanded so in the last fifty years that it now overlaps most of the various fields of medicine. The name is not entirely appropriate, but the prevention of deformity is still one of the basic principles on which orthopedic thought must always rest.

It is for this reason that we who have chosen orthopedics for our special field are vitally interested in the treatment of infantile paralysis from the very onset of the disease and not only

in the residual stages where flaccid paralysis is present and where deformity may already have developed. The diagnosis and the general treatment in the acute phase of the disease fall largely in the province of the family physician, the pediatrician, or the neurologist, and are not subjects for full discussion here, but the brilliant work which has been done with tracheotomy and oxygen therapy on bulbar cases in recent epidemics and which has saved many lives must be mentioned. It is one of the spectacular advances in the treatment of acute poliomyelitis. The orthopedist must be willing to work closely with all attending physicians and be prepared to aid and advise them and accept at least some responsibility for the prevention of deformity and the preservation and reeducation of function.

KEITH has said that "a knowledge of muscles is the beginning and the end of all orthopedic treatment," but even if we feel that this is only partly true, we must admit that when dealing with infantile paralysis, this knowledge is indispensable. Unfortunately, there is as yet no united opinion as to the physiology of muscle contraction and even as to the action of certain muscles when they do contract, but this limitation of our information must not keep us from applying what we do know from a practical standpoint to our supervision of the cases coming under our care. Let us realize at once that there is something more to infantile paralysis than the residual flaccid paralyzes and deformities which have always been assigned to the orthopedist. We must find out how these problems can be simplified by having them before us from the very onset of the disease.

A summary, in the early 1930's at one of the hospitals for crippled children with which I was connected, showed that during the ten-year period immediately preceding that time 37 per cent of the admissions had been for residual poliomyelitis and that a high percentage of these children had deformities of some type or other, many very severe, at the time of entrance. The hospital did not take acute cases,

which was true of most children's orthopedic hospitals, and therefore, the only picture of the disease which one gained at that time in such an institution was that of residual paralysis and deformity. If an orthopedist was called in during the acute stage of the infection, the treatment recommended and used was based on the classical teaching of enforcing complete rest of paralyzed muscles and preventing deformity by means of splints, frames, plaster of Paris dressings, etc., and these principles were carried on into the convalescent stage. As a result of more modern treatment, the percentage of cases in need of late orthopedic care has apparently greatly decreased.

In every epidemic a high percentage of all cases recover either completely or with very little disability, but the criterion of recovery has not been the same in all reported series. The fact that all the muscles in any particular case appear to be contracting normally does not necessarily mean that 100 per cent recovery is present, as it is also essential that all of the joints be capable of a full range of motion if that muscular action is to be completely efficient.

Residual stiffness is present in many cases who have apparently completely recovered, and this condition may lead to the development of late deformities unless it is recognized early. This stiffness is seen more often in the back than elsewhere, and it is these stiffened spines with no apparent paralysis of muscle which probably develop the curvatures that appear so unexpectedly during the first few years following an acute attack of infantile paralysis. Some so-called abortive cases undoubtedly contribute to this class, and it is possible that many of the group of scoliotics diagnosed as "idiopathic" are fundamentally unrecognized cases of non-paralytic poliomyelitis. In spite of all this, however, it is certainly true that a high percentage of individuals who have had clinical poliomyelitis completely recover, this percentage varying from epidemic to epidemic and depending very definitely, I believe, on the treatment received in the early stages.

At the other end of the list of those cases who survive are those individuals who form

the smallest group in any epidemic or series, probably rarely more than 2 per cent, and they are the ones who are completely disabled by a widespread residual flaccid paralysis. When every known procedure has been tried in these patients and all methods of treatment exhausted, the apparent uselessness of further therapy directed at the restoration of muscle power must be recognized and total disability due to irreversible paralysis accepted. Miracles do not happen to muscles after all the anterior horn cells which supply them with motor stimuli have been wiped out by the infection of poliomyelitis.

These severe cases must be nursed and cared for the rest of their lives, and this involves the economic and social factors in the individual case as well as the purely medical aspects. Supports for the body to allow easier sitting, special chairs in which the patient can be fastened, tables and rests for books and papers, special arm and hand rests, or splints which may prevent a flicker of power in a hand from being wasted, beds designed to make nursing easier, etc.; all these and many other similar appliances can be worked out by the attending physician and the orthopedist with the family and will go far in making life easier and more bearable to the individual who otherwise might be completely bedridden.

Between the two classes of patients just mentioned is another residual group, comprising probably up to 20 per cent of the individuals involved in any epidemic, in which one finds a certain amount of permanent flaccid paralysis or weakness. These are the cases which fall almost entirely into the field of orthopedics. The character of this group from the medical standpoint varies definitely with the type and thoroughness of treatment used in the earlier stages of the disease.

Deformity of some grade was the rule rather than the exception in the cases coming into our orthopedic hospitals up to fairly recent times, as already stated, and in one of our hospitals where a study was made, slightly over 50 per cent of the cases of infantile paralysis admitted in 1931 had scoliosis. The earliest that any of

these cases was seen was six weeks after the onset of the disease, and most of them had been treated by accepted methods. The other deformities present included shortening of the calf structures with a fixed equinus position of the foot, clubfoot, permanent flexion of the knees, flexion and abduction of the hips, etc. Stiffness of the back was common, and shortening of the hamstrings was found in many cases. Our work was first to correct the deformities and overcome the shortening present in some of the muscles and to start muscle training in an endeavor to get the apparently involved muscles to contract or become stronger. Later mechanical and operative treatment entered the field, as it does at present.

AT THIS point I would like to discuss very briefly why the cases which have been seen the last few years, including those from the recent epidemic of nearly 3,000 cases in Minnesota, seem to me to be in better condition when released from isolation than ever before. It has been stated that no treatment in the acute stages directed toward the muscles is of any avail and that neglected or untreated cases are just as good in the end, if not better than those receiving treatment by rest and splinting, but I cannot agree that this neglect is justified after reviewing the results of the Kenny method as carried on in Minnesota. Certainly deformities have been kept to a minimum, during the acute stage the patients have been more comfortable and the mental outlook definitely brighter, and the efficiency of the remaining muscle power has been developed and utilized to a maximum. Of course, if anterior horn cells are destroyed, they do not regenerate, and the amount of true flaccid paralysis due to this destruction is not influenced by any treatment known at the present time.

Our efforts at therapy must be directed then toward those other factors which are so prominent in the disease and which were definitely neglected or unrecognized by many of us earlier. This is no place to discuss the Kenny concept or to go into detail about the technic for

applying the ideas which make up that concept, but a very brief outline of the theory we accept and the treatment which we supervise and carry on in an effort to prevent stiffness and deformity, to overcome discomfort and pain and "spasm" of muscle, and to improve the physiology of muscles and reeducate them to resume activity is certainly in order.

"Spasm," or muscle shortening, or lack of extensibility, is present in almost every case in the acute stage, the neck, back, calf, and hamstrings being most commonly involved. This is accompanied by muscle soreness and probably is responsible for much of the pain complained of by the patient. Whether this spasm is due to direct involvement of the muscles by the disease, to neurogenic factors, or to some other mechanism is immaterial to this specific discussion, but unless it is overcome, fibrosis or permanent shortening may develop in the involved muscles, and deformity or the potential for deformity is present. It is possible that this latter condition accounts for the late development of scoliosis, as mentioned earlier.

TO DATE, the best method for relieving "spasm," or muscle shortening, is the use of very hot packs, as advocated by Miss Kenny. These are applied to the involved areas at various intervals, depending on the severity of the case, and undoubtedly act by stimulating a reflex action, as the intermittent heat with cooling seems to be far superior to continuous heat for this purpose. Packing a case properly is both hard physical work and time-consuming, and if something can be found to simplify this part of the treatment of infantile paralysis, it will be a great boon to those directly in charge of the cases. Much research is being carried on in an endeavor to find these simpler means, but as yet without any accepted success.

Several drugs have been used for the purpose of relieving muscle spasm, but the results do not seem to justify their general use or recommendation.

Prostigmine has been found useful by some observers, but it does not seem to be the answer

to the muscle shortening in infantile paralysis and cannot be recommended for routine use.

Curare, which relaxes normal muscles, has been advocated during the last few years, but also does not appear to meet the requirements for relief of "spasm" in a poliomyelitic muscle where some local condition seems present which is not always affected by the drug.

It has been reported that sympathetic blocks will relieve the pain, tenderness, and "spasm" in some acute cases of poliomyelitis, and this procedure may be a useful adjunct under certain circumstances. I have had no personal experience with it.

All cases of infantile paralysis from the acute stage to the time of discharge should be given beds which are firm and hard (ours have no springs) and which are fitted with a foot board which serves to keep the pressure of the bed clothing from the feet and allows proprioceptive reflexes to be stimulated when the feet rest against it. It is not a splint in any sense, and if the calves are in spasm, no attempt is made to place the feet against it until this has been overcome. Space is provided between board and mattress to accommodate the heels or the toes, depending upon whether the patient is lying supine or prone in bed. The knees are supported in a slightly relaxed position with the arms placed alongside the body but not against it and in the externally rotated position.

Passive motion and possibly some stretching are started early as the pain subsides and are carried out through the gradually increasing painless range until full motion is obtained in all joints. Active muscle training of a meticulous kind is begun during this time, with emphasis on coordinated movement and never on strength. Even if muscle power is apparently absent, joint motion is worked for, as there is no foundation for the fear of damaging a muscle by early motion through its full range, and this early mobilization certainly favors neuromuscular regeneration. The proprioceptive stimuli are brought out, and the active motion re-establishes the motor pattern in the brain.

Standing and walking, very carefully supervised, are insisted upon early, usually as soon

as the calves allow the feet to come to a right angle, and in this way the loss of proprioceptive reflexes is kept to a minimum, and the kinesthetic sense of the upright position is not lost. The so-called Canadian crutches are used where possible and no incoordination allowed to develop at any time.

WHERE ideal treatment has been carried out from the onset of the disease, starting with the proper positioning of the patient in bed and working through the various procedures very briefly outlined above, the end result will tend to be an individual with minimal or no deformity, with no contractures, with passively freely movable joints, and with the ultimate in coordinated function which is possible with the muscles left to that individual. Unfortunately, all cases do not receive or respond to this ideal treatment from the start and have developed stiffness and contractures when first seen, but the same general methods should be applied with the knowledge that full range of motion, especially in the back, may never be obtained.

No harm seems to be done by stretching any tightened structure, well within the limit of the patient's endurance, so as to eliminate tearing of muscle fibers during the course of treatment, but after all traces of "spasm" have disappeared. Fibrosed muscles will frequently elongate considerably with this daily stretching, and patients soon learn how to help in accomplishing this end by their own efforts. More radical treatment is sometimes necessary to overcome shortening, however, and manipulations under anesthesia and operations on fasciae and aponeuroses must be done before all contractures are eliminated. It is only when deformity is absent that the best can be obtained from reeducation and physical therapy.

During the last few years the procedure known as neurotrippsy has been developed by Doctor Billig and his associates, and it is thought by some that this operation may become a routine one in the treatment of late cases of infantile paralysis where there is resid-

ual paralysis and the return of power is at a standstill. The principle behind this method is based on the fact that if a motor nerve fiber is torn or crushed, it will tend to heal by arborization, or by sending out several branches instead of the original single fiber. These branches theoretically seek out muscle cells and, therefore, in the end increase the active nerve supply to the muscles with the result that power is increased also and the clinical picture definitely improved. As now performed, the muscles are strongly kneaded by a blunt instrument similar to an electric hand drill on the supposition that the fibers will be forcibly separated and intramuscular nerve fibers torn enough to start the arborization mentioned above. Fibrocystic areas in the muscles are, of course, broken up at the same time. Practically, there have now been enough cases with clinical improvement following this treatment to make its use a definite addition to our therapy.

When all of the indicated procedures discussed here have been faithfully followed, the number of mechanical appliances or braces needed in any specific group is reduced to a minimum, and the indications for orthopedic operations become much fewer than formerly.

There will always be a small residual group of cases (small compared to the total number in any epidemic) who will in the end require some operative treatment to lessen their functional disability due to flaccid paralysis, regardless of the excellence of the early therapy. The procedures to be used in this group are almost innumerable, and the specific nature of the operations is a purely orthopedic problem.

When the end result in any case can be accepted as probably final, the individual must be helped as much as possible to resume a normal life within the limits of the remaining disability and should have all emphasis removed from the fact that he is or has been a cripple. Patients usually experience a rather severe psychologic reaction when confronted with the diagnosis of infantile paralysis, and the emotional symptoms must be carefully neutralized if they appear. Formal psychiatric treatment is rarely needed, however.

Tumors of the Brain

ADVANCES IN DIAGNOSIS AND TREATMENT

WINCHELL McK. CRAIG*

MAYO CLINIC, ROCHESTER, MINNESOTA

TUMORS of the brain producing symptoms which are progressive present a challenge to the entire medical profession. Neurologic surgery has advanced through the cooperation of the general practitioner, internist, pediatrician, neurologist, ophthalmologist, radiologist, and every other physician who is called upon to treat symptoms of disturbances of the central nervous system. With the advancement of the technic of neurosurgery has come the realization that early diagnosis is important, and early recognition of symptoms is necessary if successful surgical intervention is to be accomplished.

During the war, although the great interest centered around cerebral trauma, neurologic diagnosis and neurophysiology received great impetus through research projects which were a part of the war effort. Now that our interest has returned primarily to intracranial neoplasms, it is interesting to note that the contributions to our knowledge of neurophysiology, as well as general physiology, antibiotic therapy, and preoperative and postoperative care, have enlarged the sphere of neurosurgery and consequently are reflected in the diagnosis and

treatment of tumors of the brain.

It has been demonstrated that if intracranial lesions are to be diagnosed earlier, physicians must be on the alert for symptoms, and in view of the fact that adult patients usually consult their family physicians and that younger patients are taken to pediatricians, these and all other consultants should maintain a suspicious attitude toward the lesions in question.

The three cardinal symptoms of tumor of the brain are headache, nausea associated with a projectile type of vomiting, and visual loss. There are many other symptoms which it would be well to mention, such as unsteadiness of gait, dizziness, unilateral deafness, roaring noises in the ear, gradual progressive paralysis, especially of one side of the face or body, unexplained partial loss of vision, causing the patient to bump into doors and other people, and unexplained convulsive disturbances which develop after adolescence.

Similar to what happens in other clinical entities which have cardinal symptoms designated as "pathognomonic," if we wait for the development of the three cardinal symptoms assigned to brain tumor, the disease is more than likely to be far advanced and therefore to be accompanied by a greater mortality rate and a lessened chance of restoring function.

The history of the patient is a very impor-

*Section on Neurosurgery, Mayo Clinic, Rochester.

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tant and significant factor in the diagnosis, for rather frequently some episode which may seem unimportant to the patient or the relatives holds the clue to the diagnosis. Of equal importance is the general physical examination, for intracranial lesions may be associated with systemic disturbances and primary malignant lesions situated elsewhere.

Roentgenologic examination of the head, thorax, and spinal column is essential. Camp and other radiologists have stressed the importance of a very careful roentgenologic examination of the head. Camp called attention to the fact that there are certain important roentgenologic signs of intracranial disease and he grouped them as follows: (1) calcification within the lesion itself, (2) localized changes in the bone, such as destruction, proliferation, or both, (3) changes in the sella turcica, (4) changes in the bone resulting from increased intracranial pressure, (5) displacement of the pineal shadow, (6) air in or about the lesion, and (7) increased vascularity of the bone.

Calcification within the lesion itself is present in only a small percentage of abnormal conditions. Such structures as the pineal body, the pliciform bodies, and the choroid plexus normally may exhibit a certain amount of calcification. Areas in the falx or the tentorium frequently described as "calcification" probably should more properly be considered as ossification. Lesions that may exhibit areas of calcification include tumors, hematomas, tubercles, cysts, old abscesses, areas of old meningitis, encephalitis, carotid arteries, and aneurysms (Figure 1). Calcification occurs in about 12 per cent of gliomas and in 70 per cent of suprasellar cysts. Cerebral aneurysms may evidence themselves by calcification in the walls.

The bones of the skull overlying a contiguous tumor may exhibit locally the change of destruction or proliferation or both. Local changes in the bone which accompany many meningiomas are rather characteristic, and consist of erosion, increased vascularity, formation of an osteoma, both localized and diffuse, enlargement of the vascular channels, and calcification.



WINCHELL McK. CRAIG

ROENTGENOLOGIC changes in the sella turcica indicate any lesion within the sella or in continuity. The lesions producing deformities of the sella turcica, according to Camp, may be classified as (1) intrasellar tumors involving the pituitary gland, (2) suprasellar lesions producing localized erosion of the sella turcica, and (3) disease of the sphenoid bone or primary conditions, both benign and malignant. Any change in the sella turcica should be suggestive of disease of the sphenoid bone, in view of the fact that changes secondary to malignant tumor extending from the nasopharynx and involving the sphenoid process are very common. In these conditions the sphenoid sinus is increased in density, and there is a haziness of the floor of the sella turcica.

In many roentgenograms of the head the pineal body is calcified, and displacement of this shadow is evidence of a space-occupying lesion. The presence of this calcified change in the pineal body is valuable in diagnosis, in that it may save the patient an encephalogram or

ventriculogram in localization of the tumor. It is well to remember that in the lateral view an area of calcification of the choroid plexus may simulate in position and shape a calcified pineal body.

In the diagnosis of tumors of the brain, the most important examination probably is a complete and comprehensive neurologic examination in which any changes in reflexes, motor and sensory abnormalities, and any deviation from the normal in posture, gait, state of equilibrium, and mental acuity are noted.

The three cardinal symptoms already referred to are produced by increased intracranial pressure, caused either by tumor of the brain or by inflammatory lesions such as arachnoiditis or abscess. Vascular lesions, such as aneurysms or intradural or extradural hematomas, may cause the same type of symptoms.

HEADACHE is the first and most common of these symptoms, although many tumors of the brain attain considerable size without producing it. More than half of the headaches resulting from increased intracranial pressure are not localized to a definite region or even to one side of the head, but are diffuse. Generalized headache caused by intracranial pressure is described as "deep and expanding"; seldom is it continuous; it occurs intermittently, usually in the morning, or every two or three days, and may be relieved by vomiting. Headache of psychogenic origin usually is more superficial, more extensive, more nearly constant and unremitting than that caused by intracranial pressure. It may be stabbing or boring, and confined to the top of the head or occipital region, producing a sense of tightness of the occipital muscles. Migraine headache may be general or confined to half of the head; it is experienced in attacks which last from half a day to four days, and is associated with nausea, vomiting and, sometimes, visual disturbances such as hemianopsia or scotomas.

The second cardinal symptom, vomiting associated with tumor of the brain, usually occurs at the peak of the headache and is follow-

ed by relief of the headache; it may or may not be associated with nausea, but it is not related to the eating of food. An explosive or projectile type of vomiting, although it is not essential, is suggestive of intracranial pressure. The relief of headache by vomiting is much more suggestive of tumor of the brain than is the character of the vomiting.

The third cardinal symptom has to do with the eyes. It may be indicated by loss of visual acuity or contraction of the field of vision. The interpretation of papilledema and changes in the perimetric fields in terms of intracranial changes has aided in early diagnosis (Figures 2a and b). Examination of the eye grounds is necessary for determination of the presence of papilledema or choked optic disk. It has been said that an ophthalmoscope is of more importance in the diagnosis of lesions of the brain than is the stethoscope in the diagnosis of lesions of the thorax.

Papilledema may be due to either increased intracranial pressure or optic neuritis. Papilledema may be present in cases of hypertension, acute and chronic nephritis, multiple sclerosis, endocarditis, diabetes, myopia, and hyperopia. Examination of the ocular fundi with the ophthalmoscope is important in determination of the presence or absence of hemangiomas of the fundi. If such lesions are found, they are almost pathognomonic of hemangiomas of the brain, usually situated in the cerebellum. A careful perimetric examination of the visual fields should be done, for early changes may indicate the site of the lesion.

Convulsions may indicate increased intracranial pressure or localization of the lesion. Tonic convulsions seem to arise from a lower level in the brain than that from which the clonic type arises. Whenever the convulsions involve one side of the face, or an arm or leg, they are of localizing value and indicate a lesion involving the contralateral motor area. Convulsive seizures occurring after adolescence which are not due to a toxic condition or constitutional disturbance should be looked upon as suggestive of tumor of the brain. Penfield and co-authors,² in a review of a series of cases,

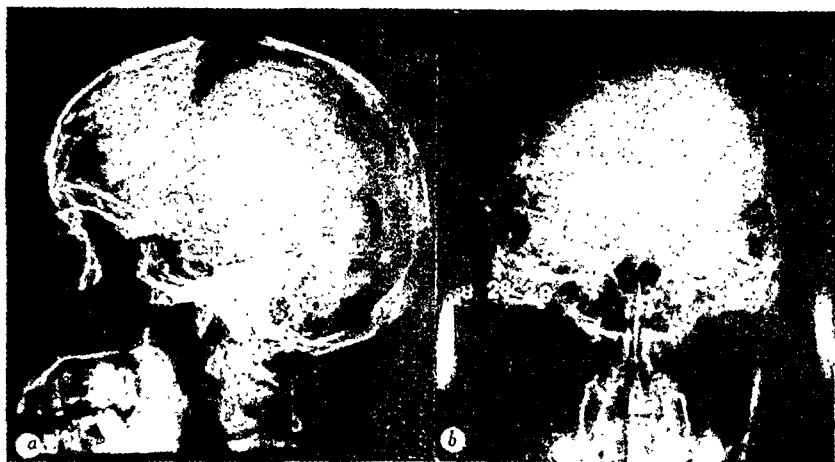


Figure 1a. Lateral view, and b, anteroposterior view, of a large calcified intracerebral aneurysm in a patient who had a history of generalized convulsions for thirteen or fourteen years, and constant headache and blurring of vision for ten years (reproduced, with permission of the publisher, from: Bancroft, F. W., and Pilcher, Cobb, eds.: *Surgical Treatment of the Nervous System*. Philadelphia, J. B. Lippincott Co., 1946).

found that when convulsive seizures were caused by tumors of the brain, they occurred in 37 per cent of glioblastomas, 70 per cent of astrocytomas, 68 per cent of meningiomas, 18 per cent of hematomas, and 50 per cent of abscesses which were checked.

It is sometimes very difficult to recognize the early symptoms of tumors of the brain in children, in view of the fact that children often complain of headache, nausea, and vomiting. Although it is true that many tumors in children are very malignant and only palliative operation can be carried out, the more benign tumors can be removed successfully quite often.

Recently a series of about 600 tumors occurring in children who had been operated upon at the Mayo Clinic was reviewed by Keith, Kernohan, and me.³ In 490 of these, the type of lesion present was confirmed by the pathologist on the basis of study of tissue removed at operation. Surprisingly enough, it was found

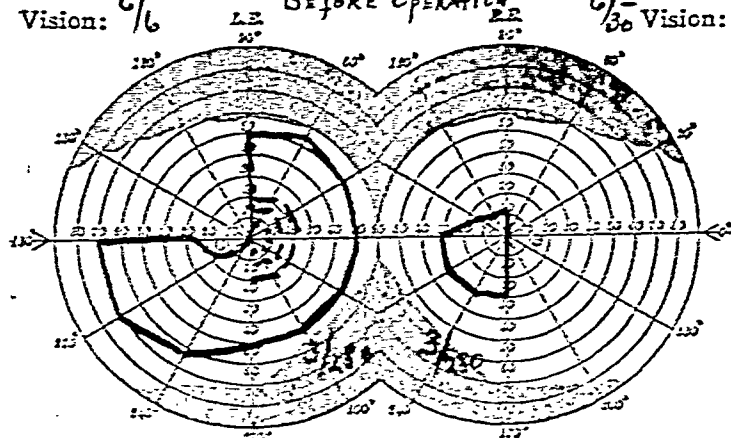
that instead of the malignant medulloblastoma, the more benign astrocytoma predominated. The cases were divided according to the type of tumor present and the length of survival of the patient after operation. Although the immediate mortality rate was rather high in the early days of the series, with the advancement of knowledge of symptoms of tumors of the brain in children, patients began to be sent to the neurologic surgeon earlier in the development of their disease. It was apparent that the early diagnosis of tumors of the brain in children allowed earlier operation, and as the years progressed not only was the mortality rate lowered but the number of one-to-five year survivals was greater. Thus, the conclusion drawn from this study was that the early diagnosis of tumors of the brain in children is associated with a greater percentage of operability, lessened morbidity and mortality rates, and a greater life expectancy.

Date. 3-29-28

Record 1. Willie.

Vision: $\frac{6}{6}$

BEFORE OPERATION.

 $\frac{6}{30}$ Vision:

a Fundi:- Pallor of both discs.

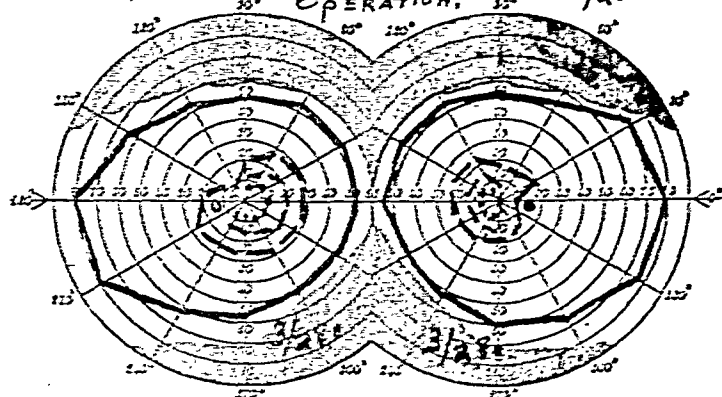
Date. 4-16-28

12 days

Record 2.

Vision: $\frac{6}{6}$

AFTER OPERATION.

 $\frac{6}{20}$ Vision:

b Fundi:- Pallor of both discs.

Figure 27. Perimetric fields, charted preoperatively, of a patient whose optic disks exhibited marked pallor; b, remarkable change in the fields of the same patient, twelve days after operation. Twelve years after operation, the fields and fundi were normal and the patient was in excellent health (reproduced, with permission of the publisher, from: Bancroft, F. W., and Pilcher, Cobb, eds.: *Surgical Treatment of the Nervous System*. Philadelphia, J. B. Lippincott Co., 1926).

TUMORS of the brain most difficult to diagnose and operate on in the early stages of development probably are the meningiomas or the benign fibroblastic neoplasms sometimes called "endotheliomas." Occurring frequently in the so-called silent areas of the brain, they may masquerade as epilepsy, diffuse headache, or change in personality. Ventriculography is required to establish a diagnosis. When these

lesions occur in the areas which subserve definite functions, they localize themselves early and, therefore, are amenable to more successful surgical treatment.

There are tumors within the intracranial cavity the early symptoms of which are not due to increased intracranial pressure but are due to pressure on certain cranial nerves or isolated areas of the brain. In this group are tumors of

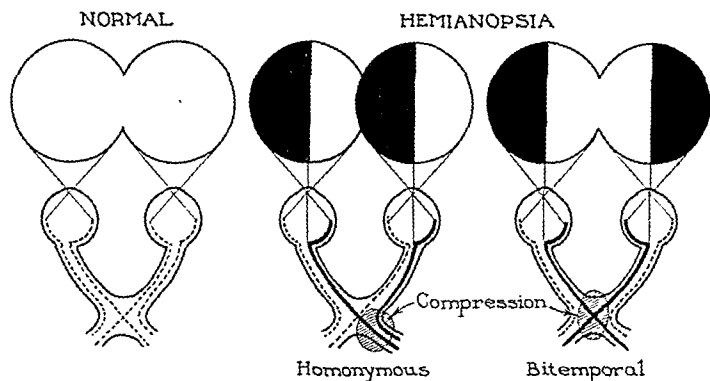


Figure 3. Schematic representation of the production of homonymous hemianopsia and bitemporal hemianopsia by lesions situated about the optic chiasm (reproduced, with permission of the publisher, from: Bancroft, F. W., and Pilcher, Cobb, eds.: *Surgical Treatment of the Nervous System*. Philadelphia, J. B. Lippincott Co., 1946).

the hypophysis and other lesions about the optic chiasm and tumors which occur in the cerebellopontine angle.

Pituitary tumors produce symptoms which involve the vision and the endocrine system. Sometimes the first indication of pituitary tumors in women is amenorrhea which is due to endocrine dysfunction. Patients suffering from pituitary tumors or tumors about the optic chiasm may complain of visual difficulties, and may undergo repeated examinations of the eyes before the lesions are recognized (Figure 3). Frequently their glasses are changed until the vision is almost lost and the optic nerves are irreparably damaged before a diagnosis is made. Then, of course, removal of the pituitary adenoma does not restore normal vision because of the development of optic atrophy. Probably in no other group of tumors of the brain is an early diagnosis so important, because if the lesion is recognized early and operation is carried out, the mortality rate is very low, the chances for recovery are better and restoration of the normal endocrine function is possible.

WHAT probably was the earliest diagnosis of tumor of pituitary gland at the Mayo Clinic was not made by a neurologist or an ophthalmologist or a neurosurgeon, but by an obstetrician. The patient came for a consultation for sterility, and when the obstetrician called attention to the amenorrhea and suggested the diagnosis, he asked for a roentgenogram of the skull. This was made. It revealed an enlarged sella turcica. Perimetric examination of the visual fields then was done; this revealed bitemporal hemianopsia which had been unnoticed by the patient until it was called to her attention. Operation was carried out in this case; the normal menses recurred, and a normal pregnancy was completed.

Tumors of the cerebellopontine angle are, in the majority of cases, benign neurofibromas which arise from the eighth cranial nerve. Meningiomas also may arise in the cerebellopontine angle, creating a series of symptoms which are difficult to distinguish from those of neurofibromas. If these tumors are not recognized early, they may grow to a considerable size, compress the cerebellum, and produce

ataxia and incoordination. By increasing the pressure within the cranial cavity, they may also produce papilledema. The neighboring cranial nerves frequently are involved when such tumors are advanced, and facial palsy sometimes develops from involvement of the seventh cranial nerve and numbness of the face and cornea develop from pressure on the fifth cranial nerve. When these tumors are recognized and operation is performed early, they can be removed with relatively little danger and, although the hearing cannot be restored, the other symptoms can be relieved. It is when the tumor has advanced and become large and produced signs of increased pressure that the mortality rate is high and the postoperative results are unsatisfactory.

Thus, it is apparent that tumors of the brain which are diagnosed early in their development are amenable to surgical treatment. This applies not only to the benign, encapsulated tumors, but also to the infiltrating malignant gliomas. However, in the early development of tumors of the brain the symptoms sometimes are so vague and uncertain that arrival at a definite diagnosis is impossible. In this event one of two courses is open, from the diagnostic standpoint. First, a patient can be kept under observation until more definite symptoms have developed or, second, encephalography or ventriculography can be carried out. Probably the greatest contribution to the early diagnosis of tumors of the brain is the injection of air within the intracranial cavity by the lumbar or ventricular routes. This procedure should be carried out only after a very careful general, ophthalmologic, roentgenologic, and neurologic examination, and never should be considered without full realization of the risk incurred.

ENCEPHALOGRAPHY, or the removal of cerebrospinal fluid and the injection of air through the lumbar route, never should be undertaken in the presence of increased intracranial pressure as evidenced by choked optic disks or papilledema. Much emphasis has been

laid on the danger of performance of lumbar puncture in the presence of increased intracranial pressure. It is even more hazardous to attempt removal of fluid from the subarachnoid space and to replace it with air.

When increased intracranial pressure is present, ventriculography, or the removal of cerebrospinal fluid and replacement of it by air from the lateral ventricles, is the operation of choice. It, also, is accompanied by a certain hazard, but this hazard is minimized when craniotomy is performed immediately afterward. Roentgenograms made after the injection of air through either the lumbar or the ventricular route furnish much information with regard to intracranial contents. A normal distribution of air in the subarachnoid space, in and around the convolutions of the cortex and within the ventricles rules out the possibility of an intracranial tumor.

Several years ago Grant⁴ reported 392 cases of ventriculography collected from members of the Society of Neurological Surgeons. Positive information as to the localization of the tumor was obtained in approximately 80 per cent of the cases. In 30 per cent definite facts as to the situation of the neoplasm were given when all other evidence was absent, and nearly 80 per cent of the tumors localized by ventriculography in the absence of neurologic evidence could be removed surgically.

One of the advances in the diagnosis of intracranial lesions has been the so-called electroencephalogram. Electroencephalography, a technic whereby the electrical activity of the human cerebral cortex is recorded through the intact scalp, has been in use for many years. Berger⁵ was the first to show, in 1929, that the electrical activity of the human brain could be detected from outside the skull. He called the record of this activity obtained with the galvanometer or amplifier and oscillograph the "Elektrenkephalogram."

The most prominent feature of an electroencephalogram of the normal human brain is what Berger called "alpha waves." These have amplitudes between 10 and 100 microvolts, and a frequency of about 10 cycles per second.

Berger also described the beta waves. These are not seen so regularly as are the alpha waves, and their origin and significance are doubtful. They appear in the frontal lobes of some subjects. The gamma waves are seldom seen, are of small size and high frequency. Berger wrote: "In cases of intracranial tumor in which the cerebral cortex is affected by invasion or proximity and where the pressure has been reduced or is still moderate, slow potential waves (10 to 20 microvolts in size, and occurring at the rate of 2 to 3 per second) have been led off from the skull over the place where the tumor was subsequently found."

ELECTRO-ENCEPHALOGRAPHIC records obtained through electrodes applied to the scalp record minute electrical potentials arising from the cortical tissue close to the electrode. These potentials vary in amplitude from 2 to 300 millionths of a volt, and in frequency from 1 up to 50 per second. These electrical potentials are thought to originate in the individual neurons, and the recorded activity to represent the synchronous beat of masses of cells discharging rhythmically and in unison. The character of the electrical activity at any one time may then be expected to be determined by the spontaneous activity of the individual neuron and by the efficiency of the synchronizing process. The individual neuron is in a state of continuous spontaneous activity, and even when presumably at rest it is rhythmically building up and discharging electrical energy. The energy for this process arises from the intrinsic metabolic activity of the cell. Within certain limits, increased metabolic activity may be expected to increase the frequency, and reduced metabolic activity to decrease the frequency. Changes in the rate, form, and, within limits, the amplitude may be interpreted, in part, in terms of the individual neuron beat.

For all practical purposes, it may be stated that certain electrical impulses are given off through electrodes from the human cortex which are transmitted to a recording apparatus which reveals certain synchronicity of the im-

pulses under normal conditions, and that any variation in the normal impulses indicates some pathologic condition.

Normal electro-encephalograms range from very rhythmic, regular, and well-synchronized records with frequencies from 8 to 12 per second to irregular, poorly synchronized records in which frequencies are not well defined, but may include faster and slower frequencies which are of low voltage. However, it has been found that under comparable conditions an electro-encephalogram of the cortex of the same person remains remarkably constant from day to day and even from year to year. There is an overall characterization, which cannot be defined adequately in terms of any such property as frequency or amplitude, that has been compared by some to the constancy of facial features, and that may be almost of identifying value for individuals.

The so-called adult norm is not reached until a person is around 13 years of age. Before this age, and, in some apparently normal children, after this age, the electro-encephalogram shows varying amounts of slow activity. This slow activity gradually diminishes and usually has disappeared by the age of 13 years. Once the adult pattern has been attained, it seems to remain remarkably constant. The only essential difference related to sex is the fact that female children seem to have a slightly faster pattern than do male children of the same age.

During the recording of the electro-encephalogram, changes in attention seem to affect chiefly the synchronizing mechanism. Thus, with the patient's eyes open, normal synchrony is disrupted by visual impulses leading to decreased regularity and the development of a low-voltage, fast pattern characteristic of a loss of synchrony.

The reduction of oxygen tension and blood sugar affects the cerebral metabolic rate, since the brain tissue, for practical purposes, may be considered to be dependent on adequate supplies of oxygen and glucose for normal metabolic activity.

It is well known that drugs affect the normal electro-encephalogram. Drugs are either

cerebral stimulants such as caffeine, benzedrine, epinephrine, strychnine, and camphor, or are cerebral depressants, such as the barbiturates, paraldehyde, chloral hydrate, ether, alcohol, and bromides. In general, the stimulants lead to increase in frequency and the depressants to decrease in frequency.

According to Reese and Masten,⁶ an abnormal electro-encephalogram in epilepsy only reproduces graphically neuronal electric potentials which, paroxysmally reaching a certain threshold, may eventuate in various clinical types of seizures, each type corresponding to certain brain-wave formations. These authors quoted the Gibbsses⁷ as stating that the various types of seizures are manifested by waves either slower than the normal 10 per second frequency or faster, 25 to 30 per second spikes of grand mal seizure. Jasper and Kershman⁸ questioned whether the type of clinical seizure can be forecast accurately from electro-encephalograms, whereas others assume that it can. A normal electro-encephalogram does not exclude epilepsy; 5 to 15 per cent of epileptic persons have normal records. An abnormal electro-encephalogram should not lead to a diagnosis of epilepsy without history and clinical evidence.

Important from the standpoint of this discussion is the electro-encephalographic localization of cerebral tumors. Reese and Masten wrote that cerebral localization of tumors of the brain by electro-encephalography is a diagnostic aid, but cannot replace entirely such procedures as angiography, encephalography, and ventriculography. Although tumors of the brain are electrically inert, the focal slow delta waves point to a regional cortical pathologic process. The electro-encephalogram is not an indicator of the number of active brain cells, and the absence of large numbers of neurons is not detectable by this electronic method.

Electro-encephalography has been investigated not only as a diagnostic aid in localizing tumors of the brain but also as an indicator as to the pathologic nature of the tumor involved. Williams and Gibbs⁹ wrote that by correlating the frequency and amplitude of path-

ologic waves with position and extent of the discharge, it was sometimes possible to surmise the nature of the lesion. Greenstein and Strauss¹⁰ reported 47 cases of gliomas and 8 cases of metastatic carcinoma. In 74 per cent of the spongioblastic tumors the focal per cent time delta was 40 or more. In 10 per cent of the transitional and in none of the well-differentiated gliomas was it 40 or more. These results seem to indicate that a focal per cent time delta of 40 or more is strongly indicative of spongioblastic or metastatic carcinomatous tumors. Reese and Masten wrote, further, that there is a definite correlation between the rapidity of growth and the percentage time wave deltas of the abnormal electro-encephalogram.

IN VIEW of the fact that I have been emphasizing the importance of early diagnosis of brain tumor to allow earlier operation, another diagnostic test which permits distinction between vascular and neoplastic lesions should be mentioned. This examination is cerebral angiography. Cerebral angiography was started by Moniz¹¹ in 1927. He was a neurologist in Lisbon, and there began his experiments in cerebral angiography. Since that time countless mediums have been used in visualization of the cerebrovascular tree by the injection of various agents into the carotid and vertebral arteries. Moniz first used potassium bromide and then sodium iodide, both of which caused serious reactions. In 1931 he used thorotrast, a material which produced roentgenograms of excellent diagnostic quality and caused little or no immediate reaction. It was found, however, that thorotrast had a high and lasting radioactivity, together with almost quantitative storage in the reticulo-endothelial system. Thorotrast is the trade name for a colloidal preparation of thorium dioxide.

Two types of damage to tissue have been shown to be caused by the radioactivity of thorium. For that reason, another medium was sought. The material finally found was called "perabrodil," and was used in Europe. It contains about 50 per cent of fixed iodine, is high-

ly soluble, and is stable in an aqueous solution. It is excreted quickly and is unchanged in the urine after it has been injected intravenously or subcutaneously. It is widely used for intravenous urograms and is called "diodrast" in the United States. Sensitivity to diodrast may develop in some persons. For this reason, preliminary ocular or intradermal tests of sensitivity should be made.

In the early tests with diodrast, 15 cc. of a 70 per cent solution was injected at one time. It was noticed that in some cases mild jacksonian convulsions occurred and that neurologic symptoms increased. For this reason, it was decided to use a less concentrated solution of diodrast. A 35 per cent solution was used for arteriograms without any evidence of adverse effect. It was found that in the lower concentration—35 to 50 per cent—diodrast is slightly less dense than thorotrast, and that it has the great theoretic advantage that the total amount injected can be much larger. By the repeated injection of small doses of a 35 per cent solution, satisfactory visualization can be obtained without the occurrence of untoward symptoms.

Ingraham and Cobb¹² reported on 25 patients ranging in age from 1 year and 10 months to 68 years who received two or more injections of 10 cc. of a 35 per cent solution of diodrast during the ensuing three years. In their summary, Ingraham and Cobb wrote: "Nineteen years have passed since Moniz introduced cerebral angiography, yet, because of its technical difficulty and its possible danger to patients this diagnostic method has not come into general use.

"Thorotrast has been the most widely employed contrast medium, although its dangers have been well known. Evidence is now beginning to appear in the literature that this material may cause sarcoma and other types of radiation damage in man as well as in experimental animals.

"Diodrast (perabrodil) is a suitable medium for cerebral angiography. It is inert in the body, quickly excreted, and highly soluble. When large quantities of a concentrated solution are used in angiography, reactions attributable to

the hypertonicity of the solution may be encountered. To obviate the occurrence of reactions, a method of injecting small quantities of dilute solutions of diodrast with a special angiogram needle is presented. . . .

"Diodrast appears to be a safe contrast medium for cerebral angiography in both adults and children when used in this way. Roentgenograms of satisfactory quality are secured and several injections may be made for stereoscopic arteriograms, for anteroposterior projection, and for demonstration of two or more of the four arterial networks of the brain."

Thus, it is seen that in the diagnosis of tumors of the brain, in addition to (1) the usual general examination, (2) the neurologic examination, (3) roentgenographic examination of the skull, and (4) ventriculography by means of the injection of air into the ventricles and the subarachnoid space, two new diagnostic methods have been developed. These are (5) electro-encephalography, and (6) angiography. Both of these diagnostic procedures have not been satisfactorily carried to completion. It is recognized by everyone using them that they are of value, if they are employed in conjunction with the history and the complete examination, but as diagnostic entities they are not at present dependable, either in the making of a diagnosis or in the ruling out of an intracranial lesion.

FROM THE standpoint of diagnosis, no evidence is brought out by the history or examination which determines the nature of the intracranial lesion. It is only at operation, when tissue is removed for microscopic diagnosis, that a definite diagnosis can be made (Figures 4a and b). At one time it was thought that a short history with rapid progression of symptoms indicated a highly malignant and inoperable lesion, but time and again patients are seen who give a short history with rapid progression of symptoms who are suffering from benign, operable, and removable lesions. At present, from the standpoint of diagnosis, it is the consensus that every intracranial lesion of which the diagnosis



Figure 4a. A normal sella turcica associated with bitemporal hemianopsia; at operation a small suprasellar cystic tumor was removed; *b*, an enlarged sella turcica, with symmetric erosion caused by an intrasellar tumor of the pituitary body. (Reproduced, with permission of the publisher, from: Bancroft, F. W., and Pilcher, Cobb, eds.: *Surgical Treatment of the Nervous System*. Philadelphia, J. B. Lippincott Co., 1946.)

is doubtful should be operated upon as early as the diagnosis can be made and localization can be ascertained. Only in this way can the operable lesion be exposed, and if a malignant type of glioblastic tumor is encountered, as radical a removal as possible should be attempted.

Not only has the development of neurosurgery been associated with improved diagnostic methods, but certain improvements in technic have been developed which have contributed greatly to the lowering of the mortality rate and the securing of permanent cures in the treatment of tumors of the brain.

Two complications in the operative recovery after the total or subtotal removal of tumors of the brain have been hemorrhage and cerebral edema. One of the outstanding recent contributions to the technic of neurosurgery has been the development of newer methods of hemostasis. For years it had been the custom of surgeons to

use autogenous muscle pledgets for the control of surface bleeding. One of the French surgeons used muscle from the breast of a dove removed under sterile conditions in the operating room. Thrombin, when applied topically, was found to have the same effect, but when it was sprayed on the surface of the brain or bleeding dura, it tended to be washed away by the seeping blood. Therefore, substances were sought for use as absorbable sponge material which could be soaked in thrombin. Three such substances were developed. A partially oxidized cellulose, which was prepared in the forms of gauze, cotton, and paper, was produced.

Although they were not the best carriers for thrombin, these substances were found to have valuable hemostatic properties in themselves, and they have been extremely useful, particularly where a small, tight pack is needed for the control of hemorrhage. Both experimental evi-

dence and clinical evidence point to the ready absorbability of this oxidized cellulose when it is used within the cranial cavity. A new processed oxidized cotton has been developed which *may prove to be a more nearly ideal hemostatic agent.*

During the war, when plasma was being processed, a by-product, fibrin foam, was discovered. This substance, when dried, proved to be a friable, porous material which absorbs thrombin readily, and which can be applied topically in the form of small pledgets. Fibrin foam can be left in place and it is not toxic. It seemed to be the logical hemostatic agent. But with the cessation of war and the decrease in the manufacture of plasma, it became difficult to process fibrin foam. For that reason, other substances were sought. It was found that gelatin can be processed into a foam-like sponge which can be rolled into various thicknesses, is tough enough to be cut into various sizes, and carries the thrombin as well as does fibrin foam. Thrombin, also a by-product of plasma fractionation, became difficult to obtain; bovine thrombin has been used in its place without any signs of toxicity. Thus, one of the newer developments of war medicine has been the production of hemostatic agents which have added greatly to the armamentarium of the neurosurgeon in the removal of intracranial tumors.

CEREBRAL edema, associated with the removal of intracranial lesions or the postoperative convalescence of the patient, has been a complication which has increased the mortality and the morbidity rates and has been a distressing factor in the convalescence of the patient. Hypertonic solutions have been used; dehydration has been used; but in almost every case there has been some reaction.

During the war a substitute for plasma was sought for use in the theaters of war. One of the by-products of plasma fractionation was serum globulin. It was found that in addition to being an adequate substitute for the use of plasma in shock, serum globulin is of great benefit in cerebral trauma as a dehydrating

mechanism. At present, serum globulin as a dehydrating agent after injuries to the head and the removal of cerebral tumors is being used and tested. The evidence now at hand would indicate that the agent would bear further investigation, because it can be used in quantities of 50 to 80 cc. with remarkable results, as evidenced in the operating room as well as during the postoperative course.

The newer developments in neurosurgery cannot be mentioned without tribute to the development of anesthesiology. In operations for the removal of brain tumors, the trend has been away from the use of local or regional anesthesia. The development of different methods of anesthesia, as well as new anesthetic agents, has accounted for this. When local or regional anesthesia is employed, patients complain of the emotional strain, if not of actual discomfort, during the operation.

It was assumed that general anesthetic agents such as ether, chloroform, nitrous oxide, and ethylene, produced increased intracranial tension and therefore were more dangerous and were accompanied by a higher mortality rate than were local anesthetic agents. However, the introduction of the intratracheal tube allowed freer use of the inhalation anesthetic agents, with a greater safety from the standpoint of both mortality and morbidity. Rectal anesthesia was accepted as a safer method for the use of anesthetic agents, and is now used in some clinics almost entirely. Intravenous anesthesia has been adopted as a safe method in certain types of operations, especially when it is produced with pentothal sodium. Pentothal sodium produces anesthesia rapidly, and the patient quickly recovers from this type of anesthesia after cessation of administration of the drug.

There is no question that the introduction of the sulfonamide drugs and antibiotic agents has created a greater margin of safety in the treatment of intracranial lesions. In addition to hemorrhage and cerebral edema, the other most-feared complication of intracranial operations probably is the development of infection. Infection which followed the removal of intracranial tumors usually proceeded to either

osteomyelitis of the skull or meningitis. Today, with the use of the different sulfonamide compounds and antibiotic agents, the incidence of infection has been reduced to almost nothing. This, however, does not mean that careful aseptic technics should in any way be abandoned; in addition to the use of such technics, which always has been strictly requisite in neurologic surgery, the use of the drugs in question is an additional safeguard against complications.

ANOTHER development in the postoperative care of patients who have undergone operations for brain tumor arose from the war. During the bombardments from the air in England, it was found that patients injured about the head must of necessity be up and about earlier than the prescribed three weeks. Patients who were injured in London were treated in first-aid stations. Because of the congestion of transportation, it was often necessary for them to be up walking about, climbing into the ambulances, coaches, and other means of conveyance. Much to the surprise of everyone, these patients did much better than the patients who had been forced to remain in bed the customary three weeks.

Thus, it was learned that patients with intracranial injuries, as well as those who had undergone operations for the removal of intracranial lesions, did much better postoperatively if they were not confined to their beds. Hence, early ambulation has entered into the postoperative care of such patients. Early ambulation has been stressed in general surgery, and early ambulation is now being stressed in neurologic surgery, to be used not only after operation for cerebral trauma, but also for intracranial operations.

SUMMARY

If intracranial lesions, and especially tumors of the brain, are suspected early and if the patients are brought to the neurosurgeon for observation and for the exercise of refinements

of diagnosis such as encephalography or ventriculography, coupled with electro-encephalography and arteriography, these lesions can be diagnosed early in their development.

Earlier diagnosis of the intracranial lesion allows for earlier operation before irreparable damage has been done to the surrounding tissues within the cranial cavity, and before the patient has been confined to his bed for a long period and his general condition has been allowed to deteriorate. All of this militates toward more successful and complete removal of the operable lesions within the intracranial cavity. It allows for more extensive resection of the less benign type of lesions; even in the gliomatous group there are cases on record in which early operation, with radical removal of the tissue surrounding the tumor, has produced survivals of five to ten to twelve years.

New additions to the diagnostic armamentarium are angiography and electro-encephalography. Although these are still in the developmental stage, they have evidenced their value in contributing to the earlier diagnosis of intracranial lesions.

REFERENCES

1. CAMP, J. D.: The roentgenologic manifestations of intracranial disease. *Radiology* 13:484, 1929.
2. PENFIELD, WILDER, ERICKSON, T. C., and TARLOV, I.: Relation of intracranial tumors and symptomatic epilepsy. *Arch. Neurol. & Psychiat.* 44:300, 1940.
3. KEITH, H. M., CRAIG, W. McK., and KERNOHAN, J. W.: Brain tumors in children. Unpublished data.
4. GRANT, F. C.: Personal communication to the author.
5. BERGER, H.: Quoted by WALTER, W. G.: The electroencephalogram in cases of cerebral tumour. *Proc. Roy. Soc. Med.* 30(pt. 1):579, 1936-1937.
6. REESE, H. H., and MASTEN, MABEL G.: Brain tumors. Year book of neurology, psychiatry, and endocrinology, 1945. Chicago, The Year Book Publishers, 1946, pp. 84 and 85.
7. THE GIBBS: Quoted by REESE, H. H., and MASTEN, MABEL G.⁹
8. JASPER and KERSHMAN: Quoted by REESE, H. H., and MASTEN, MABEL G.⁹
9. WILLIAMS and GIBBS: Quoted by REESE, H. H., and MASTEN, MABEL G.⁹
10. GREENSTEIN, L., and STRAUSS, HANS: Correlations between the electroencephalogram and the histological structure of gliogenous and metastatic brain tumors. *J. Mt. Sinai Hosp.* 12:874, 1945.
11. MONIZ, E.: Quoted by INGRAHAM, F. D., and COBB, C. A., Jr.¹²
12. INGRAHAM, F. D., and COBB, C. A., Jr.: Cerebral angiography: a technique using dilute diodrast. *J. Neurosurg.* 4:422, 1947.

Treatment of Hepatic Cirrhosis

G. O. BROUN*

ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

IN 1941 Dr. Raymond O. Muether and I reported before the Central Society for Clinical Research¹ on the successful treatment of human hepatic cirrhosis by use of a low fat, low cholesterol diet with the addition of choline. We based this therapeutic regimen on the fact that high fat, low protein diets deficient in choline produce first fatty livers and later cirrhosis in experimental animals, whereas the opposite type of diet with the use of choline may lead to recovery. We also advocated an increase in the protein content of the diet as a source of methionine in all cases with low plasma proteins. We recommended choline and methionine for their lipotropic action in clearing fatty infiltration of the liver.

The experimental studies by such investigators as Best,^{1a} Channon,² Chaikoff,³ Connor,⁴ Gyorgy and Goldblatt,⁵ Griffith and Wade,⁶ and Lillie, Daft, and Sebrell⁷ indicate that fatty liver is the antecedent event in cirrhosis of dietary origin; and that choline and methionine are of value in prevention and treatment.

This conception of the etiology and treatment of hepatic cirrhosis which we suggested has now been widely accepted.

In the years since 1941, we have had further experience in the treatment of cirrhosis. Certain additional factors have been found of value. In agreement with the observations of Kunkel, Labby, Shank, and Hoagland⁸ and

others, we have found crude liver extract of value in cirrhosis. This we reported to the Central Society for Clinical Research in November 1946.⁹

The following cases are illustrative of the use of various procedures which may influence the course of cirrhosis. The diet which we described in 1941 was relatively low in fat and cholesterol. This was based on the fact that we had produced cirrhosis in rabbits on diets high in fat and cholesterol.

CASE REPORTS

Case 1—A white female, 52 years of age, entered St. Mary's Hospital on March 5, 1939. Her previous physician stated that her liver had been palpable for several years. She developed progressive abdominal enlargement beginning in December 1938.

Physical examination revealed that her heart was not enlarged and there were no murmurs; blood pressure was 120/80; no leg edema was present. Her abdomen was distended with enlarged superficial veins, and the liver was hard, rough, and greatly enlarged. The spleen was palpable, and the presence of ascites was noted, indicated by fluid wave and shifting dullness. Her red blood cell count numbered 4,700,000; hemoglobin 14 gm. per cc.; hematocrit 43 per cent, and white blood cell count 9,100. Icterus index was 6 units, and fasting blood sugar 235 mg. per cent. The urine contained 5.0 gm. glucose in twenty-four hours.

Insulin was prescribed first on March 8, 1939, and raised gradually from 5 units three times

*Professor of Internal Medicine, St. Louis University School of Medicine; Director, Resident Staff, St. Mary's Group of Hospitals of St. Louis University, St. Louis.

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G. O. BROUN

daily to 10 units three times daily (regular insulin). On this regimen, the blood sugar fell to normal and the urine became sugar-free. Treatment with insulin was discontinued on October 6, 1939, and the diabetes remained under control as long as the recommended diet was followed.

The diet prescribed for this patient consisted of 60 gm. protein, 40 gm. fat, and 250 gm. carbohydrate.

On August 24, 1939, the liver was smaller and no ascites were present. On February 16, 1940, the liver was barely palpable, with no ascites. This patient remained well for two years and then had a relapse of diabetes due to neglect of diet. This case illustrates recovery from ascites in a case of cirrhosis on a diet low in fat but normal in protein content, without the use of lipotropic substances.

AS EARLY as 1937, Patek¹⁰ had secured encouraging results in the treatment of

hepatic cirrhosis by a highly nutritious diet rich in vitamin B complex. He used no purified lipotropic substances and gave as the basis of use of his diet merely the evidence of nutritional deficiency seen in cirrhosis. His diet was sufficiently high in protein so that it contained an ample supply of methionine and the yeast which he included contained some inositol and choline. Hence it was actually a diet which could be expected to cure fatty liver and so be of value in cirrhosis.

Patek's cases illustrated well the fact that if protein intake is sufficiently high, it is not necessary that purified lipotropic agents be used. The diets of Patek¹¹ contained from 115 to 139 gm. of protein per day. Although protein alone can be effective, we have had instances in which choline added to diets of normal protein content resulted in clinical improvement in cases of cirrhosis. It is our contention that supplementary use of choline will aid in recovery on diets of much lower protein content than would otherwise be required, as is illustrated by Case 2.

Case 2—A white female, 65 years of age, with a dietary history of anorexia and a definite dislike for protein foods, had noted some enlargement of the abdomen since June 1945. She stated that she seldom ate meat or eggs and that fried foods caused "indigestion." Her alcoholic intake consisted of two bottles of beer daily and an occasional glass of wine. In December 1946 she noted a rapid increase in abdominal distention, followed by moderate leg edema, progressive pallor and weakness.

Laboratory findings were as follows: white blood cell count, 2,550; red blood cell count, 3,560,000; hemoglobin, 8.5 gm. per cc.; no albumin in urine; nonprotein nitrogen in blood, 29 mg. per cent; blood sugar 103, plasma albumin 3.83 mg. per cent, and plasma globulin 2.91 mg. per cent. Icterus index was 12 units. The Takata-Ara test was positive in thirty minutes, and cephalin flocculation positive in twenty-four hours. Thymol turbidity was 10.5 units, with 60 per cent retention of bromsulfalein in one hour.

After paracentesis was carried out on Decem-

ber 15, 1946, a small, hard liver was felt beneath the costal margin. On December 18, 1946, a diet consisting of 65 gm. protein, 80 gm. fat, and 200 gm. carbohydrate was prescribed. This diet was supplemented with 1.0 gm. of choline chloride daily.

The patient showed marked clinical improvement and abdominal ascites cleared in six weeks, after which she remained well for four months. At the end of this time, she suffered a severe gastric hemorrhage after a period of great emotional stress, and the symptoms of cirrhosis reappeared.

MOST of our cases have been treated with low fat, high protein, and high carbohydrate diets supplemented with choline. Case 3 illustrates the effect of such a diet.

Case 3—A white male, 74 years of age, was observed in the outpatient department on March 4, 1943, and entered the hospital on March 20, 1943. His history revealed that he drank heavily up to twenty-five years ago, when he ceased drinking alcoholic beverages. He disliked and seldom ate meat, and seldom drank milk. He ate eggs occasionally, and was very fond of fried foods and butter.

Examination showed his heart to be slightly enlarged to the left. A systolic aortic murmur was noted, believed due to aortic roughening. Blood pressure was 140/80, rate 70 beats per minute. Examination of the lungs gave negative findings. The abdomen was distended; the liver was firm and somewhat rough and extended five finger breadths below the costal margin. The spleen was not felt. Shifting abdominal dullness indicated that ascites were present.

Paracentesis was carried out on March 22, 1943, and 1,800 cc. of ascitic fluid was removed. Following this, the leg edema cleared in five days. The patient's white blood cell count numbered 5,400; red blood cell count, 4.72, with 16.5 gm. hemoglobin and a hematocrit reading of 49 per cent. Prothrombin time was 60 seconds with a normal control of 34 seconds. Icterus index was 40, with prompt direct Van

den Bergh reaction. The nonprotein nitrogen was 35 per cent; blood sugar, 85 mg. per cent; blood cholesterol 160 mg. per cent; plasma albumin 2.91 mg. per cent; plasma globulin 2.31 mg. per cent; hippuric acid synthesis 0.687 gm.; bromsulfalein, only trace at 30 minutes. The Kahn test was negative, the Takata-Ara test positive in twenty-four hours.

The diet prescribed contained 115 gm. protein, 75 gm. fat, and 350 gm. carbohydrate, supplemented with 1 gm. choline chloride daily and 5 Navitol gts. two times daily.

Ascites cleared in three weeks and has not reappeared. The liver has decreased in size and the patient has remained in good health for four and one-half years.

In addition to this, some cases appear to need supplements of crude liver extract. The active substance in this liver extract is unknown. Case 4 illustrates the use of a constant diet containing 100 gm. of protein supplemented by choline and later by liver extract.

Case 4—A white male, 59 years of age, entered the hospital on September 28, 1939. He admitted a heavy intake of alcoholic liquors up to 1937, when abdominal enlargement was noted and he ceased drinking. Marked abdominal enlargement and swelling of the legs occurred in June 1939. At this time his attending physician placed him on a high protein diet. This diet improved the leg edema, but the ascites became worse and a paracentesis of the abdomen was resorted to on eleven occasions between June and September of 1939.

The patient showed no cardiac murmurs or arrhythmia. The blood pressure was 120/76. Following paracentesis, the liver could be palpated and was found to be enlarged and hard. The spleen was not felt. The superficial abdominal veins were moderately prominent. The ascites reaccumulated rapidly after each tapping, but there was no visible jaundice.

Prior to treatment, the laboratory findings were as follows: urinalysis revealed moderate albuminuria and occasional leukocytes. Just before treatment was begun, the leukocyte count was 5,200 per cubic millimeter, the erythrocyte count was 3,500,000, and the hemo-

globin was 13.7 per cc. The differential showed 60 neutrophilic segmented forms, 1 per cent eosinophiles, 7 per cent monocytes, and 18 per cent lymphocytes. The Kahn blood test was negative. Blood sugar tolerance by the Exton Rose method—fasting 99 mg. per cent, 30 minutes; 143 mg. per cent, 60 minutes; 136 mg. per cent. Hippuric acid synthesis was 2.3 gm. in a four-hour period. The Takata-Ara test was positive. The prothrombin time was 27 seconds with a normal control of 20 seconds. The nonprotein nitrogen was 35 mg. per cent, plasma albumin 1.2 mg. per cent, plasma globulin 3.2 mg. per cent, and blood cholesterol 296 mg. per cent.

At the end of September 1939 this patient was placed on a diet of 100 gm. protein, 60 gm. fat, and 250 gm. carbohydrate; this diet was maintained constantly throughout the period of treatment. During the first six weeks of treatment, no special dietary supplements were added, and the patient's condition was growing steadily worse. At the end of the first week in November 1939, choline chloride in a dosage of 1.0 gm. daily was added to the diet. A slow but definite clinical improvement followed. The accumulation of ascites which required tapping every few days decreased slightly, but progressively, from the level noted on dietary treatment alone. Appetite improved and from a nearly moribund condition, the patient was able to be up and active. Some increase in plasma proteins was also noted.

In February 1940 crude liver extract—prepared from Lilly's powdered extract #343—was given intramuscularly in a dosage of 3.0 cc. three times weekly. By August 1940 the patient was so improved that he was discharged from the hospital, and treatment was continued in the outpatient department. Choline therapy was continued, but liver extract was discontinued. The accumulation of ascitic fluid gradually lessened in the next few months and in January 1941, accumulation of the fluid ceased. The patient has remained well until the present date. Choline and liver extract both appeared to be beneficial in this case. However, complete recovery occurred in the last five

months on choline alone without liver extract.

IN 1941, Gavin and McHenry¹² showed that inositol possessed lipotropic properties, and we have also had some experience with this substance.

Case 5—A white male, 53 years of age, had noted impairment of strength for one year prior to admission to the hospital. He gave a history of beer drinking amounting to ten or more bottles per day. His appetite was poor, and his diet consisted largely of eggs, potatoes, creamed vegetables, and beer. Vomiting was a daily occurrence shortly before admission. Ascites indicated by abdominal enlargement began two months prior to hospital entry. There were no cardiac murmurs and the blood pressure was 140/70.

The abdomen was greatly distended and enlarged superficial veins were present in the abdominal wall. The liver extended 3 cm. below the costal margin and was hard and rough. The spleen was not felt. Some leg edema was present.

Laboratory findings were as follows: white blood cells numbered 6,700; red blood cells numbered 1,970,000; hemoglobin 8.5 gm. per cc.; prothrombin time was 66 per cent; blood sugar 103; nonprotein nitrogen 27 mg. per cent. The Kahn blood test was negative. Plasma albumin was 2.96 mg. per cent, plasma globulin 2.20 mg. per cent, blood cholesterol 160 mg. per cent. Hippuric acid synthesis was 0.216 gm.; the Takata-Ara test was positive in twenty-four hours; cephalin flocculation was 3+ in forty-eight hours, with 50 per cent retention of bromsulfalein in thirty minutes.

On August 24, 1944, treatment was begun with a diet consisting of 116 gm. protein, 75 gm. fat, and 350 gm. carbohydrate. In addition, two tablets of fortified yeast three times daily, two capsules of Lextron ferrous three times daily, and 1 gm. choline chloride daily were administered. In spite of this treatment, clinical improvement was slow during the following four months, and repeated paracentesis was necessary.

On January 1, 1945, the liver extract was discontinued and inositol in a dose of 1 gm. daily was added. The choline, yeast, and diet were continued. Ascites then accumulated more slowly, and after one paracentesis was done on February 8, 1945, no more were necessary and the patient made a complete recovery.

THE CASES of cirrhosis included in this report, we believe, were all of dietary origin due to low protein diets with the addition of a heavy alcoholic intake in many cases.

We have observed numerous cases of cirrhosis in cardiac cases in which prolonged passive congestion appeared to be the chief etiologic factor. Results of treatment in these cases depend on the possibility of securing compensation of the heart lesion. If this can be done, we feel that the treatment suggested for dietary cirrhosis is of help.

We have also observed a number of cases of cirrhosis developing as a sequel of hepatitis—Watson¹³ believes that these cases occur without antecedent fatty changes. We have found that these cases respond poorly to treatment with lipotropic substances. Nevertheless, we feel that the high protein diet, supplemented with lipotropic substances such as choline, inositol, and yeast, with the possible addition of crude liver extract, offers an optimum opportunity for recovery in these cases.

Cystine has been shown to be necessary for the prevention of hemorrhagic necrosis of the liver. It may also be a useful adjunct in the treatment of cirrhosis. We have not yet made studies of its use in this condition, however.

The deficiencies present in cirrhosis are often multiple, and I do not maintain that simple addition of choline is all that is needed for ideal treatment. But it appears to be one of the factors which are of value in fatty liver, and with it, success in treatment of cirrhosis can probably be attained on lower levels of protein intake than would otherwise be required. The same is probably true of cystine, inositol, and liver extract. Furthermore, any vitamin deficiencies,

e.g., thiamin, niacin, riboflavin, and vitamin A must be corrected, and there is some evidence that a rich intake of tocopherol is advisable.

It should be stressed that treatment of cirrhosis must extend over a long period of time, often many months, before success is attained in some cases. After apparent cure has been obtained, it is all-important that a highly nutritious diet, rich in proteins, be continued and that exposure to alcohol be strictly avoided. We also usually recommend the long-continued use of choline, because we have seen many prompt relapses when this regimen is neglected. We have cases who persisted in treatment and are now free of symptoms from three to five years after recovery from cirrhosis of the liver with ascites.

REFERENCES

1. BROWN, G. O., and MUETHER, R. O.: Treatment of hepatic cirrhosis with choline chloride and diet low in fat and cholesterol. *J.A.M.A.* 118:1403, 1942.
2. BEST, C. H., FERGUSON, G. C., and HERSHEY, J. M.: Choline and liver fat in diabetic dogs. *J. Physiol.* 79:94, 1933.
3. CHANNON, H. J., and WILKINSON, H.: Protein and the diet—production of fatty livers. *J. Biochem.* 29:350, 1935.
4. CHAIKOFF, P. L., and CONNOR, C. L.: Production of cirrhosis in fatty livers with alcohol. *Proc. Soc. Exper. Biol. & Med.* 39:356, 1938.
5. CONNOR, C. L.: Fatty infiltration of the liver and the development of cirrhosis in diabetes and chronic alcoholism. *Am. J. Path.* 14:347 (May) 1938.
6. GYONGY, P., and GOLDBLATT, H.: Experimental production of dietary injury (necrosis cirrhosis) in rats. *Proc. Soc. Exper. Biol. & Med.* 46:492-494 (March) 1941.
7. GRIFFITH, W. H., and WADE, N. J.: Choline metabolism—the interrelationships of choline, cystine and methionine in the occurrence and prevention of hemorrhagic degeneration in young rats. *J. Biol. Chem.* 132:627-637 (February) 1940.
8. LILLIE, R. D., DAFF, F. S., and SEBELL, W. H.: Cirrhosis of the liver in rats on a deficient diet and the effect of alcohol. *Pub. Health Rep.* 56:1255-1258 (June) 1941.
9. KUSKE, H. G., LARRY, D. H., SHANK, R. E., and HOMLAND, C. H.: Intravenous therapy of cirrhosis of the liver. *J.A.M.A.* 133:1181-1190 (April) 1947.
10. BROWN, G. O., and MUETHER, R. O.: Liver extract in the treatment of alcoholic cirrhosis. *Proc. Central Soc. Clin. Res.* 19:85, 1946.
11. PATEK, A. J., JR.: Treatment of alcoholic cirrhosis of the liver with high vitamin therapy. *Proc. Soc. Exper. Biol. & Med.* 37:329, 1937.
12. PATEK, A. J., JR., and POST, J.: Treatment of cirrhosis of the liver by a nutritious diet and supplements rich in vitamin B complex. *J. Clin. Investigation* (September) 1941.
13. GAVIN, G., and McHENRY, E. W.: Inositol, a lipotropic factor. *J. Biol. Chem.* 139:485, 1941.
14. WATSON, C. J., and HOFFBAUER, F. W.: The problem of prolonged hepatitis with particular reference to the cholangiolitic type and the development of cholangiolitic cirrhosis of the liver. *Ann. Int. Med.* 25:195 (August) 1946.
15. WATSON, C. J.: Third Conference on Liver Injury of the Josiah Macy Foundation.

Bodily Reactions of Anxiety

FRANKLIN G. EBAUGH*

UNIVERSITY OF COLORADO SCHOOL OF MEDICINE, DENVER

ANXIETY is the universal disease of our times. Probably at no other time in history were so many millions of people more conscious of the fact that anxiety is widespread, that insecurity is commonplace, and that fear of the future is a universal phenomenon. Insecurity and anxiety develop so early in life that some authors have suggested that the act of being born might be considered as an experience in which the syndrome of primary anxiety is established.

It is well accepted that early environmental factors act to frustrate, partially or completely, the child's basic drives. All children, from birth onward, have their basic drives and a desire to satisfy these urges and thus feel secure. If this is not possible, if hunger is not satisfied, if love and affection are not forthcoming, such a child will obviously show tension. Such frustrations lead to a conflict between the basic drives and the external world; and such a conflict generates anxiety. When this occurs, the drive remains in full force, and continues to seek satisfaction, but the anxiety now causes the child to repress the drive, or to seek other means of control over it.

*Professor of Psychiatry, University of Colorado School of Medicine; Director, Colorado Psychopathic Hospital, Denver.

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The method which is used to control anxiety will determine the clinical features of the personality disturbance in the patient. Although this anxiety may appear in several forms, it is important to realize that the anxiety itself is the predominant and underlying emotional reaction. In Table 1, we see the major factors involved in producing anxiety reaction.

There is also present in each of us a *normal* anxiety, that which results from adequate and known external causes that are accompanied by an element of doubt as to outcome. Such an anxiety reaction, within limits, keeps the personality alert and adjusted and is used by the ego in preparation for defense. Anxiety becomes pathologic when it recurs persistently in inappropriate situations, in reaction to inappropriate stimuli, and in response to factors of which the patient is unaware, factors which are now unconscious. Such anxiety may be either "free floating" and directly experienced and felt, or it may be unconsciously and automatically controlled by the utilization of various psychologic defense mechanisms (repression, conversion, displacement, etc.). In the somatization of anxiety, the anxiety is relieved by channeling the original conflicting impulses through the autonomic nervous system into visceral organ symptoms and complaints. These reactions represent the visceral expression of

the anxiety which is thereby largely prevented from becoming conscious.

Franz Alexander has remarked that all our emotions are expressed by physiologic or bodily processes—sorrow, by weeping; amusement, by laughter; and shame, by blushing. All of our emotions are accompanied by physiologic changes—fear, by heart palpitation; anger, by increased heart activity, elevation in blood pressure, and a change in carbohydrate metabolism; despair, by deep inspiration and expiration called sighing. In somatization reactions, the symptom results from a chronic and an exaggerated state of the normal physiology of the emotion, with the feeling or subjective part repressed. Long-continued visceral dysfunction may eventuate in structural changes.

Several reliable physicians have written that from 30 to 50 per cent of all persons seeking medical advice are suffering from emotional conflict expressing itself in bodily complaints. Medicine is no longer interested only in symptoms or in diseases of a particular organ; we are now concerned with the *person* who is sick, and how that person is reacting to his illness. We treat the patient, not the disease. The false separation between the physical person and his emotions no longer exists. We recognize our patient as a complete human being with all of his hopes, his problems, his individuality, and still living in the social world about him. In Tables 2, 3, and 4, we observe the many and variable signs and symptoms of an anxiety reaction.

WORLD War II exemplified on a mass scale the physiologic somatization repercussions of anxiety. The psychiatrist was called as a consultant to all the sections of the hospital and somatization reactions involving almost every organ and system were seen. In a combat situation the soldier was beset by multiple emotional and instinctual conflicts. His ingrained ideals of loyalty, self respect, and group feeling constantly collided through the emotion of fear with his instinct of self-preservation. Anxiety was certainly not just a mental



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state, but also a bodily one and the physical signs of disturbances of the gastrointestinal tract with vomiting and diarrhea, a dry mouth, sweating of the palms of the hands, palpitation, and tremor were not infrequently present. The emotional state resulting between his conflict of instinct for escape and desire to serve frequently became so severe that the physical symptoms became exaggerated and the soldier was incapacitated for further duty. The clinical types of anxiety are shown in Table 5.

We have come to realize that emotional stress, as well as certain physical changes, can cause palpitation, precordial pain, and transient hypertension. A patient suffering from a severe depression not infrequently manifests the biologic concomitants of anorexia, bradycardia, weight loss, decreased gastrointestinal motility, and severe constipation. Emotional impulses mediated through the autonomic nervous system are mirrored in the somatic changes involving single or multiple organ systems.

There is some clinical evidence that the hypo-

TABLE 1
FACTORS IN PROCESS OF ADAPTATION TO AN ANXIETY REACTION

THE PERSONALITY	THE SITUATION	THE REACTION
Tolerance or capacity for enduring frustration, tension, or anxiety	Social anxiety in relation to group acceptance and belonging	Anxiety-reducing mechanisms
Neurotic and immature attitudes	Educational and vocational difficulties	Phobic
Enthusiasms, loyalties, group identification, and morale versus resentments and aversions	Family and marital problems	Compulsive—obsessional and addictive
Mental capacity, intelligence, special knowledge, and skills	Establishment of independence	Depressive
	Physical disability, by infectious diseases or other causes	Hypochondriacal
	Special issues	Hysterical
		Organic fixations of anxiety (psychosomatic disorders)
		Musculoskeletal tensions
		Gastrointestinal disorders
		Cardiovascular disturbances
		Other

thalamus serves as the relay center for the conversion of emotional compulses into autonomic and endocrinologic effects. However, a tendency to overemphasize the importance of the hypothalamus in the emotional aspects of behavior has existed. It should be strongly emphasized that emotion is a highly integrated affective—autonomic—somatic reaction in which the entire organism functions as a psychobiologic unit.

The hypnotic reproduction of painful emotional stimuli can frequently experimentally produce the somatic manifestations of the illness. These manifestations are intimately bound to the sympathetic and parasympathetic nerve balance, and that of the adrenergic and cholinergic substances that mediate the nerve impulses. In an intense emotion such as fright, adrenergic responses have a generalized reaction in preparing the organism for motor activity. At the same time, more local cholinergic responses occur which are concerned with the actual muscular contractions.

Emotional excitement frequently involves both branches of the autonomic nervous system. Bulbocapnine, metrazol, and cocaine are capable of stimulating both sympathetic and parasympathetic fibers.

Myerson and his associates¹⁰ showed that the intravenous administration of epinephrine gave effects which overshadowed those produced by the simultaneous administration of mecholyl. In the application of such investigations to clinical medicine, it is possible that adrenergic

substances liberated during emotional outbursts exert an inhibitory effect on the already damaged cholinergic mechanism.

ON THE basis of experiments carried out on decorticate animals, and experiments utilizing direct stimulation of the hypothalamus, it must be concluded that it is this region that represents the expression of emotion. Sympathetic-adrenal responses predominate, but parasympathetic effects may also be obtained from stimulation of the hypothalamus. Emotion, then, may be characterized by sympathetic and parasympathetic discharges from the hypo-

TABLE 2
SPONTANEOUS COMPLAINTS OFFERED BY PATIENT WITH ANXIETY REACTION

1. Difficulty in breathing	4. Vertigo
Choking	Giddiness
Lump in throat	Swimming in head
Can't breathe in	Faint feelings
2. Precordial discomfort	5. Perspiration
Pain, pressure, and weight on chest	Cold sweats
Squeezing of the heart	Shivery feeling
(often with ill-defined radiations)	Goose pimples
3. Palpitation of heart	6. Weakness
Pounding	Knees give way
Skipping	Energy all gone
Fluttering	Paralyzed
Racing	7. Gastrointestinal disturbances
Stoppage or "heart attack"	Gas on stomach
	Gas crowding the heart
	Sick to stomach
	Epigastric cramping
	Abdominal soreness
	Diarrhea
	Flatulence

TABLE 3
COMPLAINTS REVEALED ON QUESTIONING PATIENT

1. An emotion of anxiety, manifested by: Fear of indescribable danger from within Fear of impending physical illness Fear of something unpleasant about to happen	3. Further complaints in physical state Headache Fatigue Irritability Restlessness Difficulty in sleeping Anorexia
2. Concern over mental abilities Feeling of being worried Slowing of thinking Feeling "confused"	

TABLE 4
FINDINGS ON EXAMINATION OF THE PATIENT

1. General behavior Tenseness Restlessness Uneasiness Apprehension Clothing loosened at neck	3. Cardiovascular Variable pulse rate Variable blood pressure Heart sounds often hyperkinetic
2. Skin and mucous membranes Cold, moist hands and feet Dry mouth and lips	4. Abdomen Frequently spastic Tender colon
	5. Neurologic Brisk to hyperactive muscle-tendon reflexes

thalamus. Certainly the hypothalamus may produce certain somato-autonomic changes that accompany or reflect emotion, but this is not emotion itself.

THE autonomic nervous system is arranged in the central nervous system at different levels. At times the cerebral cortex appears to possess the capacity to inhibit certain autonomic centers in the hypothalamus. Emotions or the observation of the bodily changes caused by autonomic stimulation may well arise from discharges from the cerebral cortex. The affective processes may be related especially with the frontal lobes. Frontal lobotomy may lessen or diminish emotion and its bodily manifestations. Changes in the electroencephalogram in the frontal leads are often seen early in electric shock therapy. Kennard⁸ feels that the interaction between the autonomic and somatic nervous systems with emotional display takes place mainly through the extrapyramidal system in the forebrain.

Bieber and Tarachow³ studied autonomic symptoms in psychoneurotics utilizing analytic technics and concluded that autonomic symptoms in neurotics were parts of a total attitude in which there was either a heightening or collapse of efforts at mastery. They presented clinical data to illustrate the various excitatory and inhibitory phenomena comprising the abnormal efforts in mastery or tensions and anxiety created by an inability to handle certain situations in the environment. The most com-

mon symptoms noted were sleep disturbances, conjunctival congestion, salivary and menstrual irregularities, and disturbances of skin function.

Further, there are certain types of illnesses in which emotional factors play an important role. Dunbar⁹ and French and Alexander⁷ have all done considerable original work along these lines and the following material has been summarized from some of their conclusions on the types of psychosomatic illnesses.

HEADACHE

Headache occurs in a great variety of diseases. It is not within the scope of this paper to discuss headache from an overall clinical viewpoint. The intracranial vessels are under control of the autonomic nervous system. The production of headache through reflex action from various parts of the body and in excitement and emotional states, is feasible on the basis of vasomotor changes.

In general, however, we find the emotional type of headache in patients who exhibit a characteristic type of personality.⁵ They are sensitive, tense, highly intelligent, and "highly strung," and are perfectionistic, stubborn, and often impatient with the slowness and faults of others. Such a person usually takes life seriously and feels his responsibilities keenly. He has probably always been poorly adjusted to life and had many problems, worries, fears, and compulsive ideas. Often this individual has a nagging problem which is impossible to

TABLE 5
CLINICAL TYPES OF ANXIETY

NORMAL	ANXIETY STATES	ANXIETY STATES	ANXIETY REACTIONS	ANXIETY
Resulting from adequate and known external causes that are accompanied by an element of doubt as to outcome (parent reaction to recovery or death of sick child)	Associated with or symptomatic of bodily disease, toxic condition, and organic brain changes	Arising from situational difficulties of which the person is more or less aware—i.e., "conscious" factors (often occurring on basis of constitutional-personality traits in conflict with external factors)	Arising from factors of which the patient is unaware—i.e., "unconscious" factors (often closely connected with sex instinct motivations)	Occurring in psychoses

solve and yet at the same time is intolerable to him. The main emotional feature is one of repressed hostility.

The sensitivity of the vessels in the pia mater and dura mater has shown that probably many headaches are of vascular origin, the pain being due to stimulation of the immediate nerve endings or vasodilatation. The fact that headache follows an encephalogram also indicates that more centrally located parts of the brain are also sensitive.

Simons and Wolff¹⁵ in their studies on headache feel that the prognosis on post-traumatic headache cannot be generally expressed, as much of the outcome depends on the rapport between the physician and patient and an appraisal of pre-accident emotions such as despair, frustration, anxiety, and resentment.

The exact mechanisms causing migraine headaches are not yet clear, yet a disturbance in the gonado-pituitary mechanism is to be considered and certainly emotional stress is known to precipitate attacks.

PSYCHOGENIC GASTROINTESTINAL REACTIONS

Anorexia nervosa is an old term that merely means loss of appetite on an emotional or neurotic basis. Some type of emotional upset usually precipitates the condition. Psychosomatic manifestations may include amenorrhea, low metabolic rate, and weight loss. On some occasions the clinical picture may be so severe as to remind the physician of Simmonds' disease or atrophy or degeneration of the anterior lobe

of the pituitary. An analytic interpretation of this illness usually brings out a psychosomatic illness in which fantasies of oral impregnation are dramatized through starvation, vomiting, and amenorrhea. Frequently cases with adequate intellectual capacities may respond to prolonged psychotherapeutic technics when all other attempts at treatment fail.

Therapy of anorexia nervosa is difficult if it is limited to medication. Anterior pituitary hormone is of no avail. Thyroid medication may merely cause more weight loss and the use of insulin is not indicated as a hypoglycemia exists in most cases. Bed rest, small frequent feedings, or tube feedings may help, but a resolution of emotional conflicts is essential for adequate rehabilitation.

THE act of swallowing is a complex one and central nervous tissue comprising this coordinated mechanism is therefore diffuse and extends throughout the pons and medulla. The cardia is supplied with both motor and inhibitory fibers from the vagus; however, the chief influence exerted by the vagus is probably inhibitory, but depends on degree of tone in the cardia. A spasm occurs when the sphincter does not relax properly and the patient states "I can't get food down, it sticks in my throat."

Faulkner⁶ has shown conclusively, by means of esophagoscopic examination, that suggestions of undesirable environments caused esophageal tightening and narrowing of the lumen. On the other hand, proposals of a pleas-

ant situation brought about a prompt relaxation of the spasm, and return of the lumen to its normal size. This author further demonstrated that the range of the diaphragmatic movement can be altered by suggesting imaginary situations arousing strong emotions. Pleasant emotions caused increased amplitude of diaphragmatic movement and unpleasant emotions restricted the expansion of the diaphragm. Thus cardiospasm may be related in some way to the tightening of the esophageal diaphragmatic pinchcock. It is probable then, that so-called idiopathic cardiospasm may be due to unpleasant emotional stress. At autopsy the functional stenosis has usually disappeared, but the esophageal dilatation remains.

Under the influence of anxiety and tenseness the tone of the stomach and the amplitude of the gastric contractions usually decrease. At the same time secretion of the gastrointestinal juices may be inhibited.

Pavlov's experiments many years ago on conditional reflexes demonstrated that pleasurable emotions associated with food intake may lead to the excitation of the parasympathetic system.

Brunswick⁴ attempted to correlate gastrointestinal changes with various types of emotions. He felt that in general surprise and unpleasantness were associated with an increase in tone, and fear produced a decrease in tone. These results were certainly not constant and it is not correct to state that pleasurable emotions are associated with an increased activity of the parasympathetic, and unpleasant emotions with an increased sympathetic function. Under conditions of fear, increased parasympathetic activity is often seen, such as diarrhea, increased peristalsis, and spastic sphincters.

PEPTIC ULCER

Recently increased attention has been focused on peptic ulcer and the autonomic nervous system as a result of the surgical procedure of cutting the vagus nerve. Long ago, Cushing suggested that influences arising in the parasympathetic center in the hypothalamus were

conveyed along the vagus nerves, and were responsible for changes in the gastric mucosa that led to the development of peptic ulcer. The injection of the parasympathetic stimulant pilocarpine into the third ventricle or the continued stimulation of the vagus nerve also has produced hyperemia and erosions of the gastric mucosa.

PEPTIC ulcer occurs predominantly in young men who are usually ambitious, energetic, keen, conscientious, and have a tremendous drive for success. But this individual also has underlying feelings of inferiority with consequent overcompensation and a very marked conscious drive for superiority. He has deep-seated dependency feelings and a need for affection. In some ways it is this "hunger for affection" that keeps his stomach juices overstimulated and leads to the development of the peptic ulcer.

Harris⁸ reviewed the case histories of 200 patients admitted to a military hospital for the treatment of minor psychiatric conditions. There were 25 patients who had as their chief difficulty, distress and symptoms referable to the upper gastrointestinal tract. These symptoms had appeared during some period of their military service. The emotional attitude of this group, as compared with the others, was that of conscious and freely expressed anger and resentment.

Mittelman and Wolff¹⁴ studied emotions and gastroduodenal function. Precipitating emotional factors in 30 unselected patients with peptic ulcer were guilt, frustration, resentment, anxiety, and insecurity. Situations were experimentally created which included strong unpleasant emotional feelings and these precipitated symptoms when the patient was previously symptom-free. With unpleasant feelings an increase of hydrochloric acid, mucous, and pepsin secretions were noted. The motility and mucosal activity of stomach and duodenum were also increased.

The large bowel is likewise susceptible to psychic factors and mucous colitis is frequent-

ly encountered in patients with psychogenic disturbances. This illness occurs predominantly in inhibited, possessively dependent women of 40 to 50 years of age. They usually have a long illness record, a history of several operations, and a long cathartic habit. The predominant clinical picture is one of tension occurring in an individual who is often a depressed person who broods over failures, and who has many aggressive feelings that have been repressed.⁵

PSYCHOGENIC GENITOURINARY REACTIONS

It is not surprising that the renal system should be subject to emotional stress due to its close functional relationship to the genitals. Ahronheim¹ studied emotional albuminuria under combat conditions and found the amount of albumin excreted under emotional tension fluctuates greatly but will follow a pattern which seems to be different for each individual. It was found that a combat mission represents a powerful emotional stimulus causing intermittent albuminuria. Urination is a well-known bodily expression of anxiety and usually enuresis in children is on an emotional basis. Enuresis occurring beyond the age of 10 years is a definite neuropathic trait.

The secretion of gonadotropic hormones is regulated mainly by the hypothalamus and is intimately interrelated with the autonomic nervous system.

The exact nervous pathways involved are not known at the present time. Benedek and Rubenstein² have shown that the psychosomatic unit of the mature human female is indeed a complex one and that a diversity of emotional reactions can be correlated with specific variations of hormone production.

The basic normal pattern of physiologic and personality relationships may be stated as follows: Following menstruation there is a gradual increase for ten days to two weeks of the estrogenic or follicular hormones, and paralleling this in a psychologic manner, an extratensive feeling with interest in the opposite sex. After ovulation occurs, the effects of the estro-

genic hormones are masked by the increase of the corpus luteum hormone, progesterone. Psychologically, with an increase of progesterone, flightiness, irritability, decrease in amount of interest in the opposite sex, and increased interest in the woman herself, occur. There is an emotional preparation for nidation and motherhood. During the late premenstrual period the ego becomes weak. The emotional state at this time may be often characterized clinically as a depression. Women may be somewhat retarded, sad, asthetic, indifferent, fatigued, and evidence more marked emotional lability. Psychosomatic reverberations sometimes occur during the premenstrual phase such as migraine, gastric distress, constipation, and skin eruptions. The pregnant woman is prepared both physiologically and emotionally for her motherhood and offspring. The interrelationship between emotional conflicts, the endocrine system, and the autonomic nervous system are intimate, complex, and of great psychosomatic significance.

Frigidity, sterility, amenorrhea, and low back pain are all too frequently merely psychosomatic manifestations of emotional conflict. One of the most fertile fields for further psychosomatic research is in the branch of obstetrics and gynecology.

PSYCHOGENIC CARDIOVASCULAR REACTION

THE coronary arteries are supplied by both vagal and sympathetic fibers. It would seem that the coronaries are dilated by sympathetic impulses and constricted by the vagus. The vagus, of course, acts through the liberation of acetylcholine and this substance has been demonstrated in the coronary blood during vagal stimulation. The coronary vessels have afferent fibers from both the vagus and the sympathetic. The abdominal and thoracic viscera may send reflexes to the coronaries.

The practicing clinician is well aware of the fact that anginal attacks are commonly precipitated by work or some type of emotional excitement. The pain itself is apparently due to the subsequent anoxia of the heart muscle. In managing a case of angina the clinician at-

TABLE 6
PROCESS OF THERAPY IN THE ANXIETY REACTIONS

THE AIM OF TREATMENT IS TO ESTABLISH:	ACHIEVEMENT OF THESE AIMS INVOLVES:
Appreciation of relationships	Understanding of problem
Rapport	Guidance
Emotional experience	Suggestion
Removal of causes	Emotional participation
Reconstruction	Social therapy
Emancipation	Emancipation
	Somatic therapy

tempts to soften the environment and help the patient develop a philosophy of life in which emotions may not play such an important role.

The occurrence of hypertension and hypertensive heart disease is frequent in our present culture. Such an individual usually has a high illness record, usually is married with a large family, often has other neurotic symptoms, usually had strict, domineering parents, and has seen cardiovascular disease or sudden death in his family or background. There is a life-long conflict in the sphere of authority, particularly with a fear of criticism or a fear of falling short. There is also a desire to be dominant, long-standing repressed hostility, and a tendency to resort to "wine, women, and song" in the face of stress.⁵

Wolff¹³ made day-to-day studies over a period of a year on the symptoms and cardiovascular and respiratory functions of healthy human subjects and short term observations on selected patients. He demonstrated that heart pain in the presence of narrowing of the coronary arteries may result from increased cardiac strain resulting from increased cardiac output and elevated blood pressure in association with rage, resentment, anxiety, fear, and tension. Giddiness and faintness may result from cerebral anoxia due to diminished venous return to the heart and may occur in response to stress and strain of certain emotions, such as anxiety and fear.

Weiss¹² recently reported a case of severe peripheral vasospasm affecting chiefly the lower extremities. This case failed to respond to ordinary therapy, but after six months it completely cleared as a result of one week of intensive psychotherapy. Obviously emotional and psy-

chogenic factors play a role in the course of peripheral vascular disorders. The success of surgical sympathectomy in cases of hypertension may be explained on the basis of the mechanical interruption of the autonomic nervous system—the real connection between emotions and the vascular system.

The problem of fever or hypothermia of unexplained origin is one of the most puzzling the clinician may face. Circulation plays an important role in the regulation of body temperature. Circulatory reflexes via the autonomic nervous system are influenced by varying environmental situations which call the temperature regulating mechanisms into action via the heat regulation center in the hypothalamus. Ziegler and Cash¹⁰ studied the surface temperature of 20 patients who were subjected to some emotional strain and measured the results by special technical instruments. They concluded that emotions may produce surface temperature deviations, variable in duration, even to the extent of fever or hypothermia.

PSYCHOGENIC RESPIRATORY REACTIONS

It is well known that the respirations are under voluntary control for relatively short periods of time. The nerve impulses to "hold the breath" probably arise from cells somewhere in the motor area of the cerebral cortex, hence it is not illogical to assume that the respiratory system may be strongly affected from emotional stimuli arising in the higher cerebral cortex and mediated via the autonomic nervous system.

For the past several decades it has been theorized that emotional energy could be responsible for the production of asthma, so certainly the psychogenesis of this disease is no new idea. The outstanding personality traits of asthmatic children are their overanxiety, their lack of self-confidence, and their clinging dependence on parents. Usually the family background includes a rejection of the child by one or both parents; compensation for this by overprotective and oversolicitous attitudes on the part of



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complished by virtue of inherent pulmonary elasticity.

Elasticity perishes with use and years and there is no evidence that it ever regenerates. Each individual on attaining adult growth has an equipment of elastic tissue of a certain quantity and quality: when this has been worn out by use or misuse, "he has had it." As deterioration of elasticity progresses, the recoil of the lung inevitably becomes less vigorous and less complete. This failure to spring back from the position of inspiration, this failure of systole, is the essence of the commonest form of chronic lung failure. Its far advanced stage has long been recognized as chronic emphysema.

The situation in well-advanced emphysema as compared to a normal lung is illustrated in the diagram (Figure 1). "A" represents the capacity of a normal lung at full inspiration. The shaded part is the residual air after a forced expiration. The clear part represents the total vital capacity, *i.e.*, the amount of air that can be shifted from full inspiration to full expira-

tion. This is an index of the pulmonary recoil or elasticity. "B" shows the condition in emphysema. The residual air after full expiration is much increased and the range of movement or vital capacity is correspondingly reduced. It will be seen that the total capacity of the lung is not changed. But the total amount of air in the lung while at rest is much increased and the amount of movable air is much reduced. The lung is not "blown up" or "distended" as is so often asserted. It is very little larger than it was before. It is merely unable to retract from the position of inspiration because elasticity is defective. Much of the air that it contains cannot be put into circulation; it is indeed a frozen asset.

Besides failing in retraction or recovery after distortion, a lung might lose the faculty of having its shape changed, *i.e.*, it becomes less expandable. This is produced by fibrosis. Every inflammation and every irritation of the lung initiates fibrosis. Also the passage of years sets the substitution of the vital tissues by unyielding fibrous tissues.

The effect of fibrosis on the lung, in general, has the opposite effect to that of loss of retractability. It tends to make the lung smaller rather than larger and it interferes with expansion rather than retraction. In most cases it is secondary to some other obvious condition, especially tuberculosis, repeated pyogenic invasion, silicosis, or sarcoidosis. Besides, there are cases of gradually progressive, diffuse fibrosis which appear to arise "de novo." These seem to be more common among middle-aged females.

THESE two prime causes of chronic lung failure, emphysema and fibrosis, commonly develop side by side. Since they have opposite physical effects on the lung, their signs sometimes tend to cancel one another. In spite of this, in any given case, one or the other tendency usually dominates the picture. We can commonly divide cases into those whose lung failure is due to emphysema and those in whom fibrosis is the chief factor. The follow-

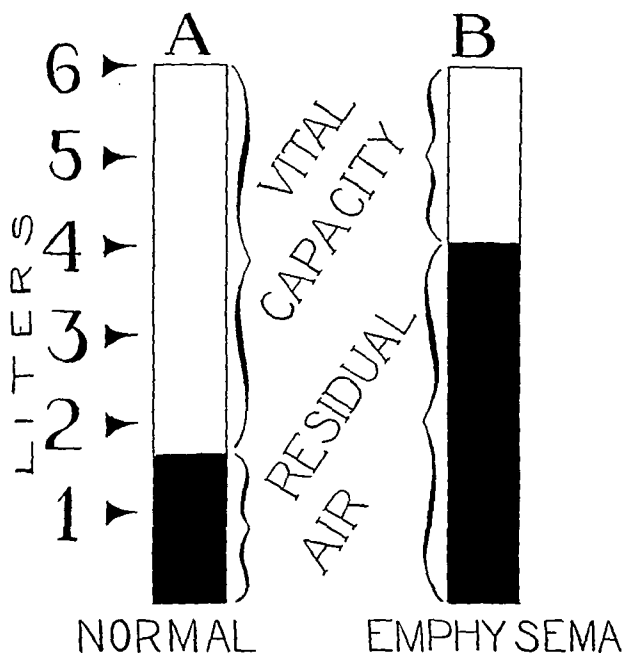


Figure 1. Situation in well-advanced emphysema as compared to a normal lung.

ing remarks will be concerned with the recognition and management of emphysema.

Clinical diagnoses, like fashions, have periods of popularity and of neglect; the history of emphysema illustrates this. Before the nineteenth century it was unknown except to a few morbid anatomists, especially Baillie and Morgagni. Laennec (1819) first established it clinically by correlating symptoms and physical signs with postmortem findings. Throughout the nineteenth century it was very much to the fore because it had such easily demonstrated physical signs. Stokes, Walshe, Rokitsky, Osler, and many other great clinicians made much of it. In our day it has definitely lost caste. The pathologists who first discovered it are still loyal and chest specialists commonly

give it some thought, but clinicians in general often overlook it. This partial eclipse of an old favorite is largely a result of the influence of radiography.

In the diagnosis of pulmonary conditions signs and symptoms have, to a great extent, been superseded by x-ray findings. This is entirely justified in the search for tuberculosis, but is an unfortunate tendency so far as other pulmonary conditions are concerned. Emphysema has been particularly neglected because radiologists have been almost completely preoccupied with the discovery and interpretation of opacities. The opposite condition—increased penetrability—unless it be localized and circumscribed, has been neglected. This is partly due to the universal custom of having

chest films made in a position of full inspiration which increases the penetrability of normal lungs and so partly spoils the contrast to those that are emphysematous. Also, the translucency of emphysema is often obscured by associated conditions—especially fibrosis and pneumonitis. As a consequence, most radiologists rarely suggest the possibility of emphysema from the film alone and, indeed, most emphysematous lungs actually appear fairly normal radiologically.

THE symptoms and the signs of emphysema are readily recognized when they are far advanced. The barrel shaped chest fixed in a position of almost full inspiration; the insistent paroxysmal cough; the marked dyspnea on effort; the recurrent attacks of bronchitis, bronchospasm, or pneumonitis, and finally right heart failure are well known. But when these evidences of far advanced emphysema appear, it is too late to do much about it. The terminal event, right heart failure, is the most discouraging type of heart failure to treat; our old standby, digitalis, is usually ineffective or harmful and such things as venesection are mere acts of desperation.

When one is confronted with such a case in a patient who is very old, one may take comfort from the stern fact that man is mortal and that time alone ruthlessly and inevitably wears out elastic fibers. But when it occurs—as it does—in those under 60, one automatically asks: "Could anything have been done to prevent this disease or postpone this evil hour?" This brings up the perennial question: "What are the early symptoms and signs?"

The older writers considered that emphysema was always secondary to chronic infection or asthma, and it is, of course, true that either of these will contribute to its production. It is also true that there is emphysema which is primary, comes on insidiously, and is commonly overlooked until complicated by infection or spasm. This primary lung failure can be recognized—if thought of—before gross complications have developed.

In Manitoba we have had an excellent opportunity to study this question. In the early days of the present century we had a large immigration of peasant farmers from Galicia and Bukovina, provinces in the extreme southwest of the old Ukraine. Before and since coming to Canada they worked at the most arduous labor. Many of them are now in the sixth and seventh decades of life and for some unaccountable reason emphysema is exceedingly common among them. Our hospital wards at all times have several far advanced cases. In them the development of emphysema can frequently be traced as a primary lesion—the so-called bronchitis and asthma being quite definitely secondary.

Unfortunately, for early diagnosis, the first symptoms are so insidious in onset that the patient, over the years, adjusts himself to them and often accepts them as natural for his years.

TABLE I

DYSPNEA OF EMPHYSEMA	CARDIAC DYSPNEA
Very gradual onset (five to ten years)	More sudden onset (months)
Always worse in winter and cold air	Not necessarily so
Usually normal rate	Tachypnea common
Obvious expiratory difficulty	No special expiratory effort
Dyspnea apparent to observer	May be inconspicuous
Not very distressing	Usually accompanied by anxiety or fear
Not paroxysmal or unprovoked (unless asthmatic)	Spontaneous nocturnal attacks
No obvious cardiovascular signs	Other objective signs of cardiovascular disease

Dyspnea is the cardinal symptom and emphysema cannot be diagnosed in its absence. It begins in the fourth or fifth decade and develops slowly. As a rule the patient accepts it as a sign of aging. He will often realize that his work is "too hard for his age" and will make some job adjustment. If he complains and is examined at this stage, the gradually increasing dyspnea is most frequently mistaken for cardiac dyspnea. If there is some hypertension—which is more common among em-

physematous patients than others—this inference is strengthened. If there is no hypertension, cardiac arteriosclerosis is often invoked as a cause. This may commonly be supported by minor electrocardiogram changes often interpreted as "myocardial strain." The points that differentiate these two common sources of dyspnea are brought out by a searching history. Table 1 presents the contrasting features.

NONE of these points is alone sufficient to distinguish these two common forms of dyspnea. By considering all of them it is usually possible to form a sound opinion as to the chief source of the dyspnea. In general, one can say that pulmonary dyspnea is objective and cardiac dyspnea is subjective. Pulmonary dyspnea is clamorous and arrests the attention of the observer; cardiac dyspnea is silent but it completely preoccupies the patient. When cases are far advanced and there is an element of right heart failure, it becomes most difficult or impossible to estimate what part of the dyspnea is from each source. In general, in such circumstances the pulmonary contribution is underestimated. Much significant emphysema may be discovered among the patients in "heart clinics" and emphysema is frequently an unexpected autopsy finding.

Bronchospasm ultimately plays a part in the dyspnea of emphysema. Many patients finally have definite paroxysms from slight provocation. In fact, it is true to say that asthmatic attacks coming on after middle life most commonly have emphysema as their main cause.

Cough appears with the dyspnea or soon afterwards. It may be the first symptom of which the patient takes heed. It has several distinctive features by which it may be recognized. These are: (1) much out of proportion to expectoration; (2) spasmodic and paroxysmal (paroxysms uncontrollable and produce cyanosis, dyspnea, and sometimes vomiting); (3) brought on by effort, cold air, dust, or laughter (paroxysms commonly occur on first arising); and (4) each cough prolonged and gusty—with emphasis on expiration (the op-

posite to whooping cough).

Expectoration is always scanty or absent for a long period in primary emphysema. Ultimately defective drainage is followed by chronic inflammation and more profuse expectoration and sometimes secondary bronchiectasis.

This history of insidious dyspnea associated with unproductive spasmodic cough is usually present in patients with this type of lung failure, but it is rarely given spontaneously. There is no condition in which the patient is so casual about his symptoms. His family—especially his wife—will commonly tell you much more than he will about his cough and dyspnea.

Loss of weight is sometimes surprising in its degree and rate.

Fatigability also may be one of the presenting symptoms. These two latter symptoms may occasionally be so striking as to arouse a strong suspicion of tuberculosis or malignancy in the minds of both patient and doctor. Even though the disease is essentially very slow in its progress, urgent symptoms may appear quite suddenly in some cases.

The diagnosis can be supported by definite physical signs. In far advanced cases these may be discovered on a very cursory examination. They may be enumerated as follows: (1) general undernourishment; (2) varying degrees of cyanosis; (3) thorax nearly fixed in position of inspiration; (4) reduced movements and epigastric pulsation; (5) percussion sometimes gives hyperresonance; (6) weak breath sounds, prolonged expiration, and rhonchi; and (7) myotatic irritability. Minor degrees of these signs are found in less advanced disease.

A plethora of other signs have from time to time been described. As with many other diseases, the multiplicity of alleged signs tends to make the diagnosis appear more complex than it really is. In a patient with symptoms as described, one needs to demonstrate only two to secure the diagnosis. Since the fundamental defect is loss of elasticity, the most dependable physical sign is reduction in movement of the thorax. This can best be tested by the oldest method—palpation. By standing behind the patient and placing the fingers in the intercostal

spaces one may analyze the movement. If the lung is normal one can feel the rubbery expansile thrust during deep inspiration. In emphysema this sensation of vigorous inflation disappears and the thorax feels as though paralyzed at the top of inspiration, appropriately called "frozen." This simple maneuver to test movement is better than radiography or vital capacity estimations—though these may be used for corroboration, if it is convenient.

THE second important physical change is the characteristic contour of the thorax. This change from the normal to the so-called barrel shaped chest produces a multitude of minor signs, e.g., high square shoulders, short neck, horizontal ribs, wide epigastric angle, and many others. All of them may be expressed in a simple mathematical statement, namely the "thoracic index."

As the lung loses elasticity it becomes more globular; the anteroposterior diameter becomes greater. The usual anteroposterior diameter is in the neighborhood of 20 cm. The largest anteroposterior diameter in normal people is rarely over 24 cm. Paul M. Andrus¹ believes that anything over this figure means certain enlargement. This is by no means always the case and very large people who have normal lungs may have anteroposterior diameters up to 25 cm. The transverse diameter in normal people is in the neighborhood of 30 cm.—the usual variation is from 26 to 36. The thoracic index (e.g., the anteroposterior diameter/the lateral diameter) is therefore normally about 0.7 and varies from 0.6 to 0.75. As emphysema increases the chest becomes deeper and this figure increases. Any figure over 0.75 almost certainly means emphysema. In far advanced cases the figure may be 1.0 or more; that is, the thorax is deeper than its width.

These measurements are readily made with a pair of obstetric calipers with the patient in an upright position. The largest diameter in each direction is used in determining index;

care must be taken to hold the calipers horizontally. Any deformity of the chest primarily due to disease of bones renders these measurements valueless.

These two simple physical signs—reduction in movement and increase in thoracic index—are the most dependable evidences of beginning lung failure. Their discovery in elderly or middle-aged people can give a most valuable clue to the explanation of beginning deterioration. They will indicate the true cause of much dyspnea, now vaguely attributed to "myocarditis" or cardiac arteriosclerosis.

Unfortunately most chronic lung failure that we see is already far advanced when diagnosed. Patients too often complain only after the inevitable complications have made life unbearable and treatment must usually be directed against these complications and not against the primary disease. The treatment of these complications—namely, bronchospasm, gross sepsis, and right heart failure—is purely palliative and will not be considered here.

By being on the alert for the characteristic symptoms and the beginning signs, especially increased thoracic index, one is sometimes able to make an early diagnosis. What should be the management of such a case? Is there anything substantial to be done to postpone complete disability?

In thinking of the preservation of lung elasticity it is helpful to make an analogy to the elasticity of an inner tube. The length of its life depends on: (1) the quality of the material originally put into its composition, (2) the amount of actual trauma that it has suffered, and (3) the variations in pressure to which it has been subjected.

The survival of lung elasticity depends on precisely the same circumstances.

1. The quality of the elasticity with which lungs are endowed at birth varies widely between individuals, families, and possibly races. In practice there is not much one can do about this except to recognize these tendencies and take special precautions. For example, in the Galicians to whom I have referred, the first possibility when one of them begins to fade

¹ANDRUS, PAUL M.: *J. Canad. M. Services* 3:6 (September) 1946.

out is always lung failure. Similar tendencies have long been recognized in some families. The discovery of such cases in the incipient stage demands a complete investigation of the patient's activities in the hope of eliminating lung stress. This may mean a complete change of occupation or the renunciation of futile physical efforts at "keeping young."

2. All trauma to the lung hastens deterioration just as blowouts finish a tire tube. Trauma comes in the form of repeated inflammation. With the universal use of the newer drugs there is no doubt that secondary lung failure due to smoldering infection will be much reduced. A wider use of these drugs in subacute and chronic pulmonary inflammations would contribute to the prevention of lung failure.

3. In emphysema that begins without such provocation (apparently primary) can we do anything to prolong elasticity? Can we reduce the frequency and violence of sudden changes of intrapulmonary pressure? This is caused naturally by hard manual labor which involves straining with the glottis closed. It accounts for the fact that most emphysema is found in laboring males. Medically we can do no more about this than we can prevent deterioration in the tire tubes of trucks that must carry heavy loads. Industrially it seems to be solving itself since hard manual labor is fast becoming quite out of fashion.

THERE is one thing I think we can do. That is reduce the amount of useless coughing. Frequently abnormal coughing is to the lung what a rough road is to a tire. A great number of people accept a morning and evening paroxysm of coughing as normal. It is so common

in practice that we, too, are inclined to minimize it if we find none of the well-known pathologic conditions. In the presence of cough these should be sought for by every means at our disposal, including radiology, bronchograms, bronchoscopic examinations, and particularly a searching examination of the upper respiratory tract. Also allergy should be considered. In the absence of these, the commonest cause is cigarettes. I am convinced that anyone with an otherwise unexplained cough should immediately give up cigarettes. If, besides coughing, they are beginning to have slight dyspnea and signs suggesting emphysema, it is imperative—just as important as for the man with angina or peripheral vascular disease. The results in chronic cough are usually most striking—though it may require several weeks of abstinence to show them.

SUMMARY

1. Chronic lung failure is common in those past middle life.

2. It is due to fibrosis, which is secondary to chronic inflammation or to deterioration of elasticity (emphysema).

3. Emphysema is frequently a primary condition and not necessarily secondary to infection or asthma.

4. It is usually recognized after secondary infection, bronchospasm, and right heart failure have produced total disability.

5. It may be recognized early by a detailed history of symptoms and by discovery of reduced movement and increased thoracic index.

6. If recognized early, its progress might be retarded by taking precautions against "wear and tear" on the elastic tissue of the lung.

DIAGNOSTIC CLINIC

The Medical Management of Hyperthyroidism

DANIEL L. SEXTON*

ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

THE MEDICAL management of hyperthyroidism includes that group of patients treated wholly without surgery and those patients who ultimately have surgery but require careful preparation. Agents available for treatment of this disease include the goitrogenic drugs, the iodides, x-ray, and radioactive iodine.

X-ray has been used for many years by direct application to the gland without very encouraging results. However, it may be considered as a method of treatment when other measures fail in the very difficult cases. There have been very few permanent remissions reported following the use of x-ray directly to the gland.

Another form of x-ray therapy is its application to the hypophysis. Thompson has reported that in a series of 43 patients there were remissions in about two-thirds. The mechanism by which this works is the suppression of the thyrotropic fraction of the anterior hypophysis. We have used it in a few instances where there has been that so-called persistent type of hyperthyroidism, with symptoms persisting after surgery, in which both iodides and the goitrogenic drugs have failed. We have ap-

plied x-ray to the hypophysis, but not with very encouraging results.

Radioactive iodine is still in the experimental stage. Although prepared by Fermi in 1934, it was clinically used for the first time in 1942 by Hamilton and Lawrence, who reported its use in three cases. In 1942, Chapman and Evans reported that in a series of 22 patients they had favorable results after one dose in 14 and less favorable results in the other 8. There were some complications from the use of radioactive iodine. Myxedema occurred in four patients; they had evidence of radiation sickness in six; and there was fibrosis of the gland in two in which the gland was biopsied.

Radioactive iodine promises a great deal. It is a nice form of treatment for the patient, for it is given in a single dose, but until its full effect is determined its use must remain in the hands of those investigators who have proper facilities. Its effects on the other structures of the endocrine system and its effects on the organism as a whole are as yet not fully understood, so for the present it must be carefully controlled; we must keep abreast of developments, for the results as reported to date are indeed very promising.

This leaves us, then, the use of the goitrogenic drugs and the iodides, which I believe

*Assistant Professor of Clinical Medicine, St. Louis University School of Medicine, St. Louis.

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are of the greatest practical importance. Since the advent of the goitrogenic drugs there has been a revived and a keener interest in the medical management of hyperthyroidism. This is due to the fact that surgery has not fulfilled all the requirements necessary for the adequate treatment of this disease. Arguments that surgery completely cures exophthalmic goiter may go on, but many of us who practice the medical side of medicine know that there are many problems following surgery with which the surgeon never is troubled. He often does not see the patient after the latter leaves the hospital. There are many problems in the management of hyperthyroidism that have not been solved by thyroidectomy.

Chemical compounds that possess antithyroid properties fall into two general categories: (1) those that act without producing goiter, such as iodine and radioactive iodine; and (2) those that produce hyperplasia of the gland and at the same time suppress thyroid function. These latter drugs are referred to as goitrogens, and include the cyanides, thiocyanates, sulfonamides, thiourea, and derivatives of thiourea. The antithyroid and goitrogenic effects of cyanides and thiocyanates are of experimental interest but not of great clinical significance. Experimental work on the cyanides, however, laid the groundwork for the development of a great deal of the present knowledge of the physiology of thiourea derivatives.

In 1942 Kennedy determined that the active principle which caused goiter in cabbage-fed rats was thiourea, or allyl thiourea. With this information, Astwood studied a large number of compounds, variations of thiourea, and concluded that thiouracil was the most effective derivative at that time. Since Astwood's original work on the use of thiouracil in man, several thousand hyperthyroid patients have been treated and observed.

The toxicity of thiouracil limited its widespread use. Continuing his search, Astwood and his co-workers isolated 6-propyl thiouracil, which has been found to be effective in dosages of 30 to 50 per cent that of thiouracil. At the present time propyl thiouracil is the drug of



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choice when this form of therapy is employed.

THE TWO figures give some idea of the effects of thiouracil. I think that Figure 1 is self-explanatory. In the upper left corner is a diagram of normal thyroid relationships, the pituitary-thyroid relationship. Normally there is stimulation from the emotional centers of the brain. The cause of exophthalmic goiter or Graves' disease is not fully understood, but it is believed to be due to a severe emotional upset. If we assume that these emotional stimuli arise within the brain, they then come down to the pituitary and stimulate that gland. On your left of the two-armed arrow is that stimulating portion that causes growth of the gland; on your right is the arm that affects the uptake of iodine and the ultimate formation of the thyroid globulin.

The thyroid globulin is composed of several elements: diiodotyrosine, thyroxine, and other amino acids. Unless the globulin contains thy-

roxine, the other elements do not have the effect that we normally think of as the thyroid-stimulating effect.

In the arm to your right you see that the thyroid hormone, designated as TH, is formed. It has an inhibitory effect on the pituitary and on the production of the thyrotropic fraction; it also has an inhibitory regulatory effect on the amount of thyroid globulin that is formed. With this fine mechanism in proper relationship, there is just the exact amount of thyroid hormone formed to keep the body metabolism normal. That relationship is designated by the effect on the body tissues, the BMR, which is representative of normal thyroid function.

If we look at the diagram on hyperthyroidism we see an increased stimulation from the emotional centers coming down to the hypophysis. This increased stimulation reflects in an increased production of the thyrotropic hormone, which in turn affects the gland proper and produces further hyperplasia. As a result, the thyroid gland is larger than it is under normal circumstances.

The right arm causes an increased uptake of iodine from the blood. With this increased uptake of iodine there is an increased formation of the thyroid hormone. This increased formation of the thyroid hormone makes an attempt to regulate the production of thyrotropic hormone, but its attempt is inadequate, and this increased stimulation continues. It also attempts to go around and regulate the amount of thyroid hormone that is formed, but again it cannot overcome the excess stimulation from the thyrotropic fraction. This process results in an increased metabolism in the body tissues, which shows up in an increased metabolic rate.

The lower diagram indicates what happens when the thiourea derivatives, thiouracil or propyl thiouracil, are employed. The amount of stimulation from the hypophysis is the same as it was in hyperthyroidism. The thyrotropic fraction which has had this increased stimulation comes down and increases further the hyperplasia of the gland. That is true theoretically, and practically it is true in about half the instances in which thiouracil or propyl

thiouracil is used. The gland enlarges probably in half the instances; in just as many it does not enlarge, or may even become smaller.

The thiouracil effect, however, is chiefly on the right arm. It blocks out the formation of the thyroid hormone within the gland proper. There is an enzyme system that is necessary for the production of the thyroid hormone, and when this block is placed within the gland proper there is a reduced uptake of iodine from the blood, i.e., there is a blocking out of the formation of the thyroid hormone. When this occurs, the original inhibitory effect as shown in the first diagram is lost. As a result, the pituitary stimulation goes on uninhibited, the thyroid hormone is not formed, and the basal metabolic rate drops very low.

THE indications for thiouracil therapy are (1) preparation of the patient for surgery (more will be said about that later), and (2) the nonsurgical treatment of hyperthyroidism.

There have been very few reports on permanent remissions with propyl thiouracil, mainly because the drug has not been used for an adequate length of time. With thiouracil, however, the drug was used and withdrawn and in some quarters permanent remissions were reported in about 50 per cent. That was not our experience with thiouracil. Before using propyl thiouracil we used thiouracil in 44 patients and we thought we had a good many permanent remissions. As time went on, however, these patients would come back to us either with a spontaneous recurrence or with a recurrence following some other systemic disease, many times after an upper respiratory infection. Thus we believe that permanent remissions following the use of thiouracil will prove to be relatively few.

Propyl thiouracil has been used now for about eighteen months, and we feel that we have not used it long enough to make any report. However, in those instances where the patient has dropped out of sight for a period of time and then returned, or when, for some reason, the drug had to be withdrawn, there

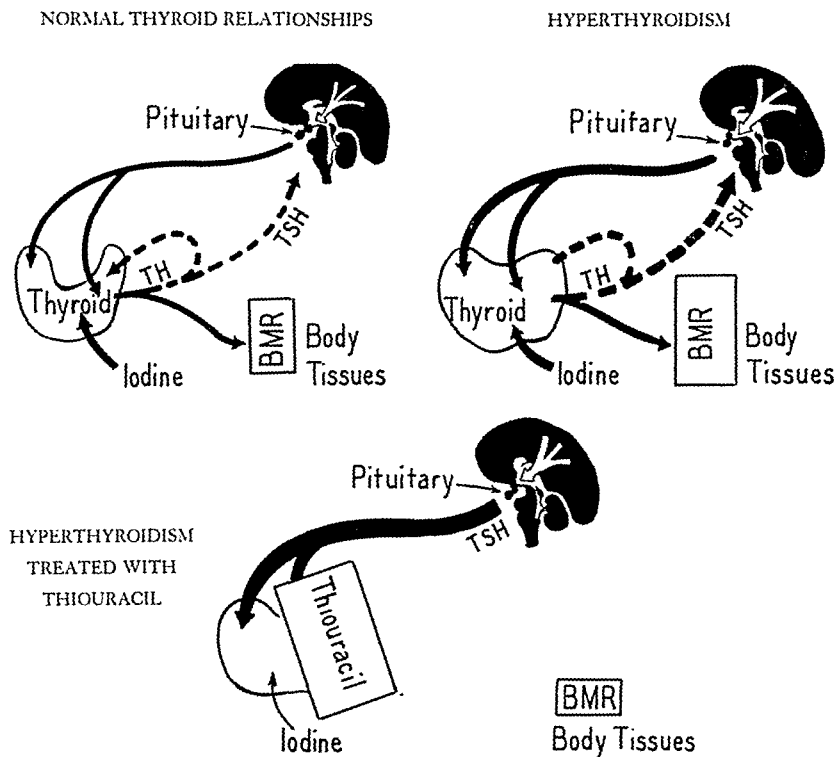


Figure 1. Suggested pituitary-thyroid relationship in normal, hyperthyroid, and thioracil (or propyl thioracil) treated patients.

has been a recurrence of symptoms, but those patients were not given the treatment over a prolonged time. We have felt that we ought to carry this treatment out for at least eighteen months, and we are now just beginning to take our earlier patients off the drug.

Recurrent hyperthyroidism is oftentimes an instance where thioracil or propyl thioracil is to be employed for reasons which I am sure

are well understood: the patient does not desire further surgery, is disappointed, and fears a recurrence, so if we can control him we feel that he is entitled to that plan of treatment.

We feel definitely that the treatment of hyperthyroidism of pregnancy should be carried out medically if it is at all possible. As you know, that is quite a problem with the iodides.

Agoitrous hyperthyroidism is a form in

which propyl thiouracil may be employed. It is valuable since there is always some question as to the diagnosis in these cases. The proof comes in the response of the patient.

Finally, as a therapeutic test it is valuable in those unusual cases that offer a great deal of trouble diagnostically as to whether the patient is of the anxiety type with an acute emotional upset or whether the patient is truly hyperthyroid.

Because of toxic reactions from this drug we should proceed in its use if not with extreme caution, certainly with careful observation. Thiouracil was toxic to the extent of about 14 per cent. The most serious reaction that came from thiouracil was, of course, leukopenia, which was less than 1 per cent, but there were other reactions that totaled about 14 per cent. The reactions that did occur with thiouracil and that can occur with propyl thiouracil are leukopenia and eventually agranulocytosis (there were cases of agranulocytosis and death with thiouracil), jaundice, purpura, fever, urticaria, morbilliform rash, edema, diarrhea, submaxillary and parotid involvement, and alopecia areata.

The propyl thiouracil reports indicate that toxicity measures about 6 per cent in the dosages that are employed, which are up to 300 mg. a day, so it is a much less toxic drug. At this time it is the drug of choice.

I do not want to imply that the iodides are not still of great value, for they are; they play an important part in the treatment of hyperthyroidism. If a patient is being prepared for surgery and is in a mild state of toxicity, the iodides—some form of iodine—are the drugs of choice, because the patient can be prepared in a relatively short time. Propyl thiouracil, on the other hand, requires some six to eight weeks for preparation.

THE patient, however, who is profoundly hyperthyroid had best be prepared with propyl thiouracil because the basal rate can be brought down to a much lower level—down to normal and below normal—if the dosage is

increased and carried out over a sufficient period of time; and it definitely reduces the incidence of thyroid storm. Lahey reports that they have had no thyroid storms in a large series of cases since the thiourea derivatives have been employed.

If a patient is prepared with propyl thiouracil, iodine should be added from two to four weeks before the operation. By so doing, the hypervascularity and the hyperplasia, the friability of the gland that results from the use of this drug, are overcome.

Iodine may be used in the treatment of hyperthyroidism when the patient is intolerant to propyl thiouracil, and shows reactions to it. In the treatment of thyroid crises iodides may prove lifesaving.

The following cases have been treated chiefly with propyl thiouracil.

The first case is that of an adolescent boy, with a diffuse enlargement of his gland. This 10-year-old boy had been coming to the pediatric clinic at Desloge Hospital since birth. Because of the exophthalmos and the enlarged gland, Graves' disease has been suspected right along. He would come in, however, only for other disorders, and the diagnosis was never fully established though attempts were made to get a basal and to study him carefully. However, he came to the endocrine clinic in May 1947. The result of several basal rates was ± 27 per cent, and the pulse rate was 120. At that time he weighed 53 pounds. He was placed on propyl thiouracil, 50 mg. daily for the first week or two, and then the dosage was stepped up to 100 mg. daily and has been maintained right along. On October 10, 1947, his basal rate was -22 , pulse rate 82 to 92, and his weight 63 pounds.

The boy is much calmer; his school work, of course, has improved because he can now pay attention, and he has shown the improvement that would be expected with a basal rate of -22 .

This boy is not hypothyroid with a basal of -22 . That basal is probably normal for him, and for that reason the ± 27 was not indicative of the severity of his thyrotoxicosis.

DIFFUSE TOXIC GOITER
ST. LOUIS COUNTY

H. G. \pm 19
46-4692

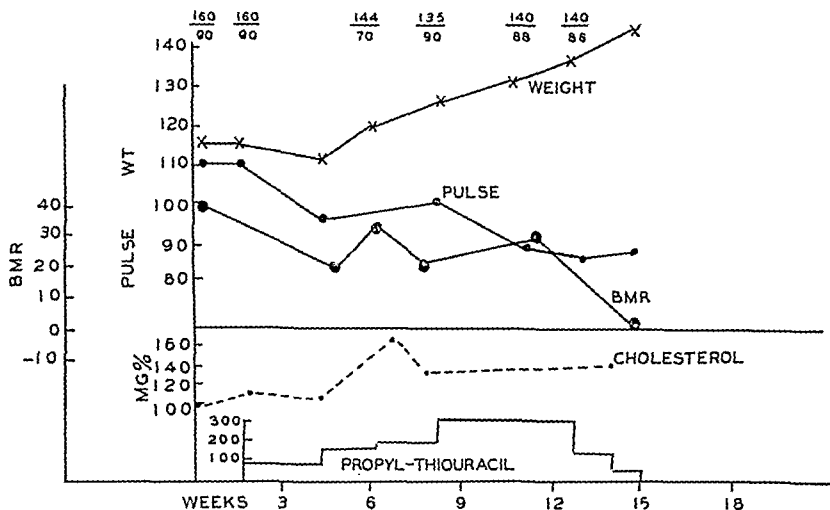


Figure 2. Diffuse toxic goiter in 19-year-old girl who showed maximum response to treatment after thirteen weeks.

(Observed on the medical service of Dr. J. P. Murphy.)

We think that adolescent children should be carried through their adolescence on medical treatment. The thyroid gland plays a very important part in the control of the endocrine system, and during the period of adolescent awakening, the growth and development of the child and his emotional stability will be much better controlled if it can be left intact.

In the second case, the patient, a female 47 years old, shows a small nodule in the right lobe. This lady came to us in July 1947 with a history of having lost 25 pounds over a three months' period and of being extremely nervous. She had a slight tremor, but none now.

Her basal rate in July was +51 per cent. She has been on propyl thiouracil since that time (a total of forty-eight days) and on October 6, 1947, the basal rate was -10 per cent. She has gained 6 pounds. Of course she has an improvement of her symptoms, as designated by the basal metabolic rate.

Oftentimes the weight gain that you would expect is lacking. When propyl thiouracil is used, the basal rate is suppressed rather definitely in the exophthalmic type in about six to eight weeks on the average. In the adenomatous type, a little longer period is necessary before adequate results are obtained.

THE THIRD patient is a lady who entered St. Louis City Hospital in March 1947. She is 64 years of age. She had been treated on the outside for cardiac disease and was sent in with the thought that her illness was due to a cardiac break. When she entered the hospital in March she was semi-conscious, extremely restless, and her tracing showed auricular fibrillation. The blood pressure at that time was 160/50. As she was examined and studied, she was found to have prominence of her eyes and a definite enlargement of her thyroid gland. It was felt that her trouble was not solely that of cardiac decompensation but that she had thyrotoxic crisis.

She was given iodides intravenously (sodium iodide and glucose). She showed some improvement on the second day, although she says that she does not remember the first five days in the hospital. It was about the fifth day when we felt that she was going to get along all right.

The iodides were continued on this patient. On the ninth day a basal determination was made, and it was ± 48 per cent. Iodine was continued for a period of three weeks, then discontinued, and propyl thiouracil was instituted. She has been on propyl thiouracil since about the first of April.

She went home, came back to the outpatient clinic, was carried along on treatment, and early in September it was decided that surgery would be the best plan of treatment for this lady. She has continued to show fibrillation. She takes 2 cat units of digitalis daily. Since

March she has gained 30 pounds in weight. Her basal rate within the past week was ± 11 per cent, her blood pressure is 138/85. She is up and around and we feel that she is ready for surgery. She has had iodine the past three to four weeks and we do not anticipate any thyroid storm. We anticipate a perfectly normal, uneventful operation, such as has been our experience in those patients that have been operated after treatment.

Figure 2 graphically shows the effect propyl thiouracil had on a 19-year-old girl who was first treated with Lugol's solution. When she was first seen she had a basal rate of ± 37 per cent, the pulse rate was 132. She was treated with Lugol's solution for about ten weeks. They were dissatisfied with the benefits obtained and the patient dropped out of sight, but came back to this physician some sixteen weeks later, when she was referred to us. At that time her basal rate was ± 65 per cent, her weight was 120, and her pulse rate was up around 160.

She was placed on thiouracil and the dosage built up to 0.6 gm. per day. You can see the drop in her basal rate. It took about sixteen weeks for this girl to come down to normal, and with thiouracil she was suppressed to -26 .

We have not been able to suppress the basals on our patients as profoundly with propyl thiouracil as with thiouracil. It is because of the dosage. We use 200 to 300 mg. a day of propyl thiouracil as our average dose, though there are instances when it will have to be stepped up to 400 or even 450 mg. grams to obtain the proper results.

CORRECTION

In the article, "Bacteriologic, Etiologic, and Serologic Studies in Epilepsy and Schizophrenia, III," published in the May issue of *Postgraduate Medicine*, the legends for Figures 3 (p. 374) and 4 (p. 376) were transposed.

Congenital Anomalies
of the
Heart and Great Vessels

*Clinicopathologic Study
of 132 Cases*

Part I

T. J. Dry • J. E. Edwards • R. L. Parker
H. B. Burchell • H. M. Rogers
and
A. H. Bulbulian

MAYO CLINIC
ROCHESTER, MINNESOTA

AUTHORS' FOREWORD

THE GREATEST advances in the recognition of congenital cardiac defects have been made through the correlation of clinical and laboratory data with the findings at necropsy. It was with this thought in mind that the authors of this publication re-examined all the specimens of congenital cardiac anomalies which had been collected in the Section on Pathologic Anatomy of the Mayo Clinic over a period of some twenty-five years. From this study an exhibit was prepared, the purpose of which was to portray by models, photographs and drawings the structure of these specimens and to correlate the clinical features with the anatomic lesions. In preparing our exhibit we chose for presentation representative cases about which we had the most complete information. As is well known, a certain physiologic derangement which will produce cyanosis can be caused by a variety of anatomic anomalies. Also, there may be great variation in the symptoms and signs of patients who have a given type of cardiac malformation and, therefore, we have listed, with each case presented, the more common clinical features of that particular anomaly.

The exhibit thus prepared was presented at the centennial meeting of the American Medical Association held in Atlantic City in June, 1947. To the original data included in this exhibit we have added reproductions of portraits of pioneer investigators in the field of congenital heart disease. We selected those whose writings have greatly influenced our ideas; other students of congenital heart disease might have chosen differently. Moreover, it is not our intention to convey the impression that the influence exerted by any one of these individuals is necessarily limited to the lesion with which his or her portrait is associated.

We have studied additional cases which have since become available to us and we have modified our data in respect to the incidence of the various types of anomalies accordingly. Apart from these additions and changes, the material presented here is essentially that included in the original exhibit.

This material is being presented in *Programs and Medicine* in two sections, the first of which appears herewith. The second and concluding part will be published in the October issue of the Journal.

It should be pointed out that in some of the cases there was more than one primary defect of the heart or great vessels. Such cases have been listed under the heading of the most serious type of defect present. The incidence of atrial septal defect and of Eisenmenger's complex may be clarified by this further definition. We included under the heading of "atrial septal defect" only those cases in which the abnormality gave rise to signs, clinical or morphologic, of increased cardiac load. Under the heading of "Eisenmenger's complex" we included those cases in which the aorta straddled the ventricular septal defect to any degree and in which there was associated right ventricular hypertrophy and a pulmonary artery of normal or greater than normal width.

It is with much pleasure that we express our indebtedness to those who have been of assistance to us in the preparation of both the exhibit and this publication. Dr. J. W. Kernohan, head of the Section on Pathologic Anatomy, was responsible for the suggestion that the study, of which this is a report, be done. Mr. Russell Drake was especially helpful in preparing schematic drawings; members of the Photographic Department of the Mayo Clinic were painstaking in their efforts to obtain the best possible photographic representation of our material. We are indebted to the W. B. Saunders Company for permission to republish portraits of Thomas B. Peacock, William Harvey, Jean-Baptiste de Senac, Franklin Paine Mall, James Hope, Edienne-Louis Arthur Fallon, and John Baptist Morgagni; to the executors of Maudie Abbott's estate to republish portraits of Maudie Abbott and Karl Rokitsinsky and to Mr. Thomas E. Keys, Librarian, of the Mayo Clinic, for his efforts in procuring photographs of some of the historical figures which we have reproduced in this publication.

Cor Biloculare

(Two-chambered Heart)



WILLIAM HUNTER

1718-1793

In a report of three cases (*Med. Observations and Enquiries*, 1784), William Hunter described pulmonary atresia and pulmonary stenosis associated with ventricular septal defect. His emphasis upon the inadequacy of pulmonary blood flow in determination of the extent of the disability is modern. His clear description of the attacks of unconsciousness associated with dyspnea and cyanosis may be called a classic.

Cor Biloculare

(Two-chambered Heart)

THIS is the most primitive heart in our series. It has a single atrium, a single ventricle and a common atrio-ventricular valve. A single functioning arterial trunk, the aorta, leaves the common ventricle.

The pulmonary artery lies behind the aorta and is atretic. The circulation to the lungs is by way of a patent ductus arteriosus.

The common atrium receives blood from the lungs through the pulmonary veins, and peripheral blood through the inferior vena cava and a right, as well as a persistent left superior vena cava. This anomaly frequently is associated with isolated dextrocardia.



Fig. 1—Left anterior view (model x1).

(1) Aorta arising from common ventricle. (2) Atretic pulmonary artery. (3) Persistent left superior vena cava. (4) Left pulmonary artery.

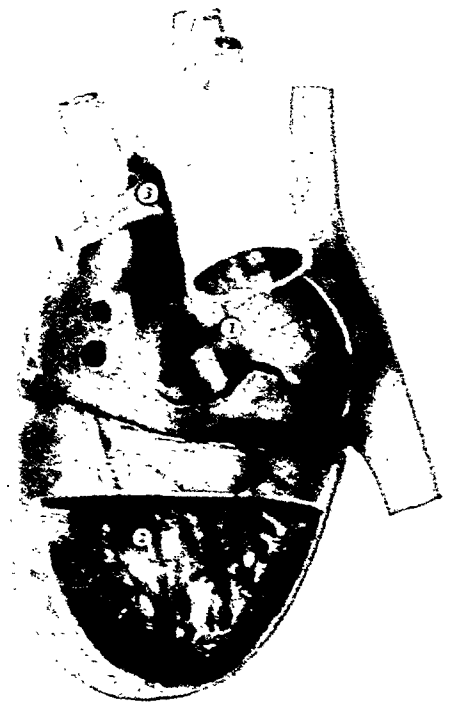


Fig. 2—Left posterior view (model x1).

(1) Rudimentary septum in common atrium. (2) Interior of common ventricle. (3) Patent ductus arteriosus.

History of the Patient

FEMALE. 8 months old. History of cyanosis, since birth, on feeding or crying. No murmurs. Hemoglobin 20.7 gm. per 100 cc. of blood. Admitted to hospital for repair of diaphragmatic hernia. Roentgenogram of thorax showed diaphragmatic hernia and prominence of right upper border of the heart. Cyanosis increased post-operatively; the patient died later the same day.

Principal Clinical Features of this Anomaly

1. Early and progressive cyanosis.
2. Characteristically, no murmurs.
3. Early cardiac enlargement of globular shape.
4. Usually, death in infancy or early childhood.

Incidence in this Series—One patient, aged 8 months.



Fig. 3—Specimen from which model shown in figures 1 and 2 were prepared. Interior of common ventricle and aortic orifice.

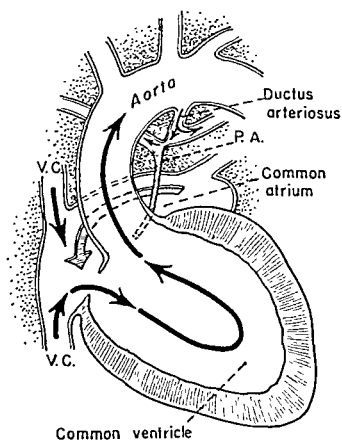


Fig. 4—Diagram of intracardiac circulation in cor biloculare with atretic pulmonary artery and patent ductus arteriosus.



Fig. 5—Thoracic roentgenogram of the patient whose heart is illustrated in figures 1, 2, 3 and 4.

Cor Triloculare Biatrium

(Three-chambered Heart)



THOMAS BEVILL PEACOCK

1812-1882

Among the various small yet very comprehensive monographs published near the middle of the nineteenth century, that of Peacock is probably best known. The clinical and pathological correlations and the very clear illustrations are probably the best and most nearly accurate up to that time. In particular, the illustrations of the anomaly now called the tetralogy of Fallot are beautifully presented.

Cor Triloculare Biatrium

(Three-chambered Heart)

THIS is a three-chambered heart with two atria and a single ventricle. The latter represents a primitive state in which there is no ventricular septum. There is transposition of the aorta and pulmonary artery, as shown by the right anterior position of the aortic origin. In this specimen, there is isolated dextrocardia. Functionally, this heart varies little from a two-chambered heart, since there is a free mixture of venous and aerated blood in the common ventricle.

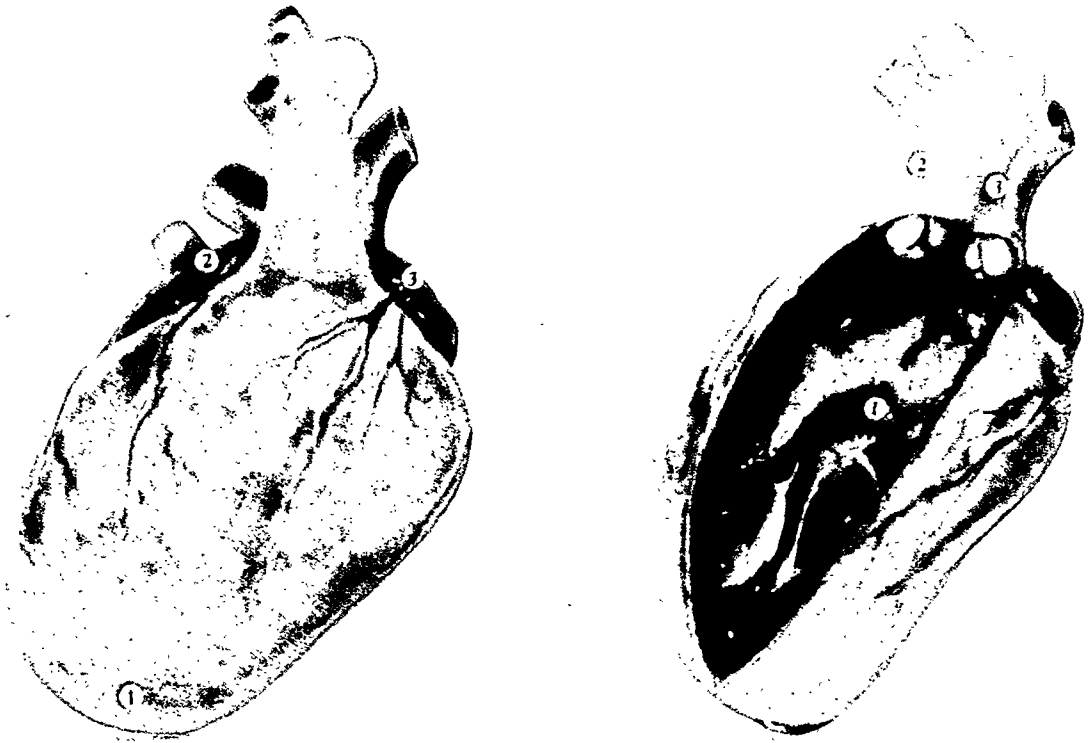


Fig. 6—(left). Anterior view (model x1). (1) Apex of common ventricle directed to the right. (2) Right atrium. (3) Left atrium.
Fig. 7—(right). Interior of common ventricle (model x1). (1) Common ventricle. (2) Aorta arising anteriorly. (3) Pulmonary artery arising posteriorly.

History of the Patient

FEMALE, 10 months old, well until age of 5 months. Then a "cold" developed with fever and respiratory difficulty. At 7 months, cyanosis was noted which became more intense at 9 months. Patient was admitted with pneumonia and congestive heart failure. Roentgenologic study revealed isolated dextrocardia with marked cardiac enlargement. Hemoglobin, 17.5 gm. per 100 cc. of blood; erythrocytes numbered 5,710,000 per cubic millimeter. Cyanosis increased markedly before death.

Principal Clinical Features of this Anomaly

1. Cyanosis develops early, but may be mild or transient and intensified by activity. The oxygen saturation of arterial hemoglobin always is subnormal.
2. Systolic murmur over the entire precordium usually is present.
3. Oxygen saturation of hemoglobin in ventricular blood exceeds that of hemoglobin in mixed venous

- blood (cardiac catheterization).
4. Roentgenologic aspects: unusual globular configuration (the most frequent anomaly associated with isolated dextrocardia).
5. Electrocardiogram: usually high voltage diphasic QRS complexes.

Incidence in this Series—Five cases.

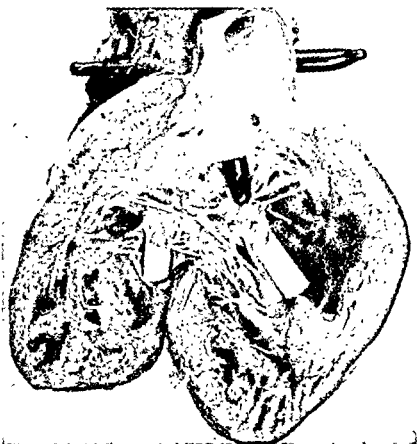


Fig. 8—Specimen from which models shown in figures 6 and 7 were prepared. Interior of common ventricle and origin of aorta.

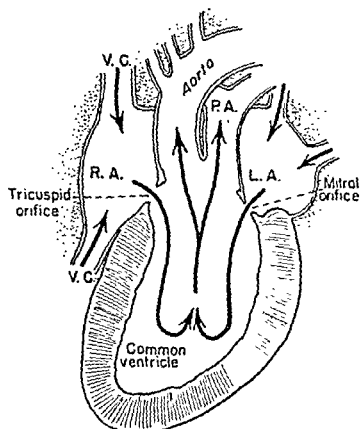


Fig. 9—Diagram of intracardiac circulation in cor triloculare biatrium.

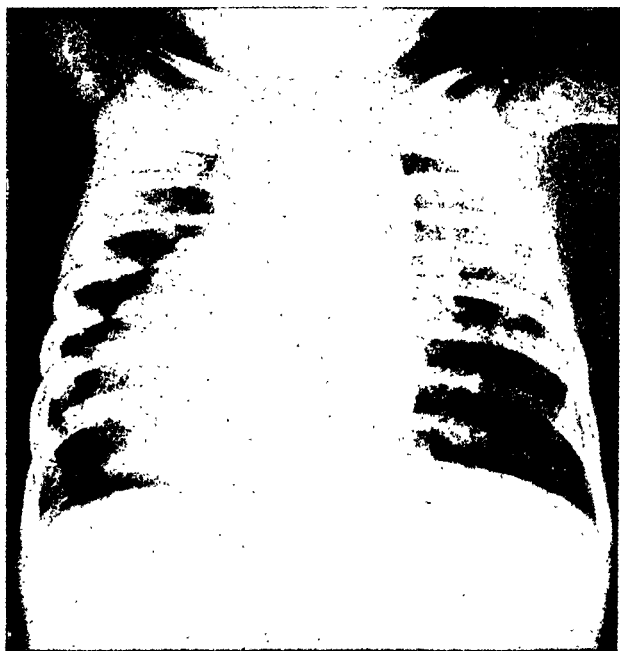
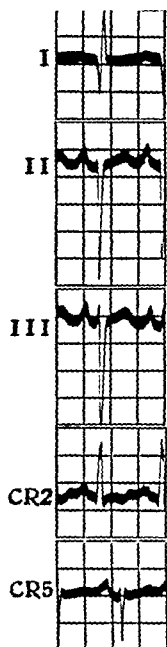
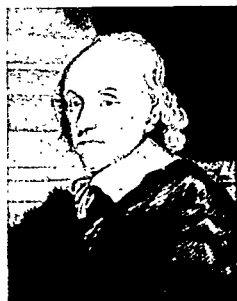


Fig. 10—Electrocardiogram and thoracic roentgenogram of patient whose heart is illustrated in figures 6, 7, 8 and 9.

Atresia of Tricuspid Orifice

(Functional Two-chambered Heart)



WILLIAM HARVEY

1578-1657

On page 46 of "Exercitatio anatomica de motu cordis et sanguinis in animalibus," 1628, appears such a clear description of the fetal circulation and the flow of blood through the foramen ovale that a student of congenital heart disease should have this classic work as required reading. "So, in embryo forms, whilst the lungs are idle and have no action or motion (as if there were none at all) nature makes use of both ventricles of the heart, as if one, for transmission of blood."

Atresia of Tricuspid Orifice

(*Functional Two-chambered Heart*)

IN THIS heart there is no communication between the right atrium and the right ventricle. The foramen ovale is patent.

The right ventricle is diminutive and communicates with the large left ventricle through a slit-like defect in the ectopic ventricular septum. The pulmonary artery is narrower than the aorta. The ductus arteriosus is closed.



Fig. 11—Anterior view (model x1).
(1) Large left ventricle. (2) Diminutive right ventricle.
(3) Pulmonary artery.



Fig. 12—Interior viewed from right (model x1).
(1) Patent foramen ovale, the only outlet of right atrium.
(2) Large left ventricle. (3) Diminutive right ventricle.
Probe is inserted through ventricular septal defect.

History of the Patient

FEMALE, 4 months old, had transient cyanosis at birth, more apparent at 5 weeks of age. Basal systolic murmur. Readmitted at 10 weeks of age. Same murmur present; moderate cyanosis; hemoglobin 17.7 gm. per 100 cc. of blood; erythrocytes, 5,170,000 per cubic millimeter. Roentgenogram: globular enlargement with absence of shadow of pulmonary conus and diminished hilar markings. Electrocardiogram: left axis deviation. At 4 months, right hemiplegia developed. Patient readmitted in coma and died. Thrombosis of longitudinal and transverse venous sinuses, with left cerebral infarction.

Principal Clinical Features of this Anomaly

1. Progressive cyanosis from birth.
2. Severe spontaneous dyspneic attacks have been noted in some cases.
3. Usually, basal systolic murmur.
4. Roentgenologically, cardiac enlargement. Configuration may resemble that in tetralogy of Fallot.
5. Electrocardiogram: left axis deviation, an important diagnostic feature.

Incidence in this Series—One patient, aged 4 months.



Fig. 13—Specimen from which models shown in figures 11 and 12 were prepared. Interior of right atrium.

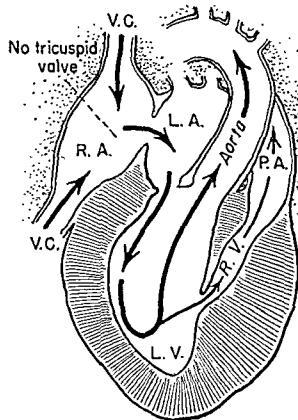


Fig. 14—Diagram of intracardiac circulation in atresia of tricuspid orifice.

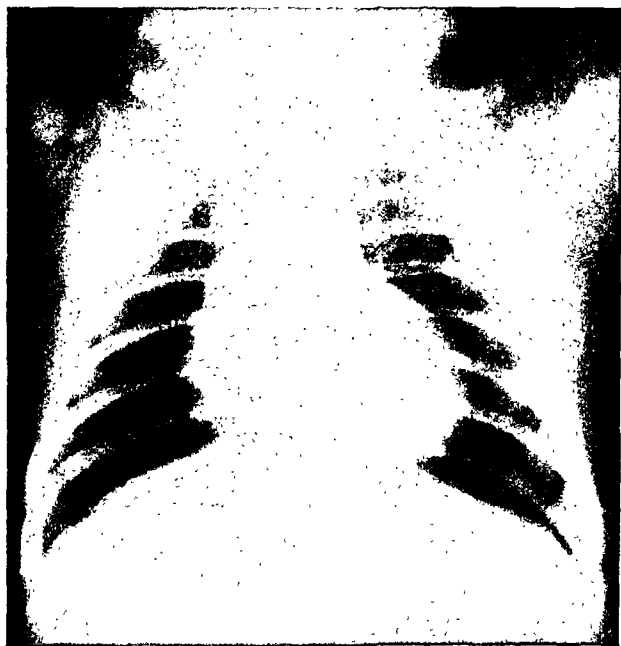
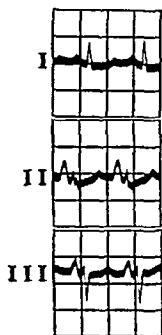


Fig. 15—Electrocardiogram and thoracic roentgenogram of the patient whose heart is illustrated in figures 11, 12, 13 and 14.

Atresia of Mitral Orifice

(Functional Two-chambered Heart)



JEAN-BAPTISTE DE SÉNAC

1693-1770

In de Sénac's detailed clinicopathologic studies of diseases of the heart, "*Traité de la structure du cœur, de son action, et de ses maladies*," there appears a thorough discussion of the fetal circulation and a short discussion of the congenital anatomic defects of the heart. De Sénac has been credited (Abbott) with having first associated *la maladie bleue* with absence of the ventricular septum.

Atresia of Mitral Orifice

(*Functional Two-chambered Heart*)

IN THIS heart there is no communication between the left atrium and left ventricle. The foramen ovale is patent.

The left ventricle is small and communicates with the larger right ventricle through a defect in the membranous portion of the ventricular septum.

The aorta arises anteriorly and to the left, and is slightly narrower than the pulmonary artery. The ductus arteriosus is closed.

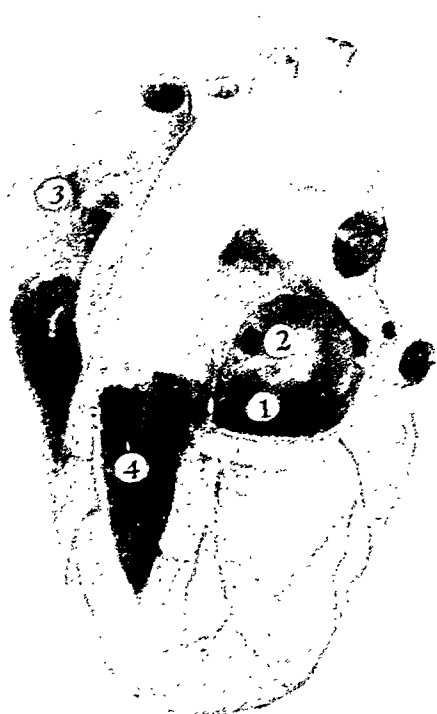


Fig. 16—Left lateral view (model x1).
(1) Atresia of mitral orifice. (2) Patent foramen ovale.
(3) Large right atrium. (4) Small left ventricle.

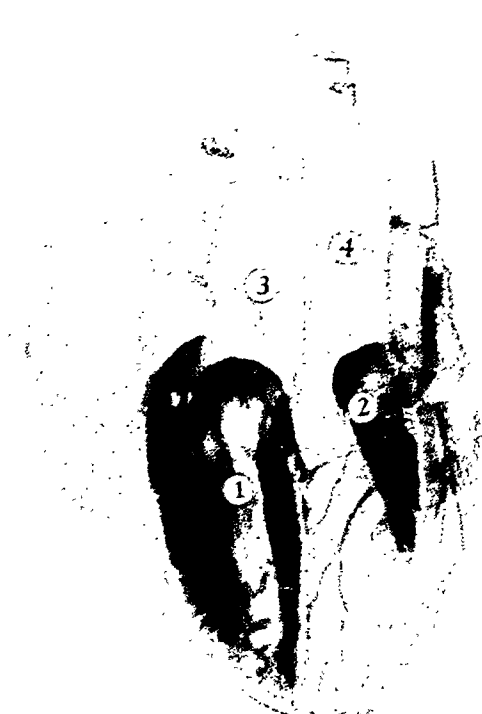


Fig. 17—Anterior view (model x1).
(1) Large right ventricle. (2) Small left ventricle.
(3) Pulmonary artery. (4) Aorta.

History of the Patient

MALE, 4 months old. Loud systolic murmur noted at birth. Slight intermittent cyanosis, beginning at 2 months of age. Child represented a feeding problem, with poor development. On final admission, loud systolic murmur and thrill were noted over entire precordium and interscapular area. Roentgenogram showed marked cardiac enlargement; the electrocardiogram, right axis deviation. Severe terminal cyanosis with pneumonia occurred.

Principal Clinical Features of this Anomaly

1. Progressive cyanosis.
2. Precordial systolic murmur.
3. Death in infancy or early childhood.
4. Roentgenologic aspects: marked right ventricular

enlargement and prominent shadow of pulmonary artery.

5. Electrocardiogram: right axis deviation.

Incidence in this Series—Three patients: one newborn, one 3 months old and one 4 months old.



Fig. 18—Specimen from which models shown in figures 16 and 17 were prepared. Interior of left atrium.

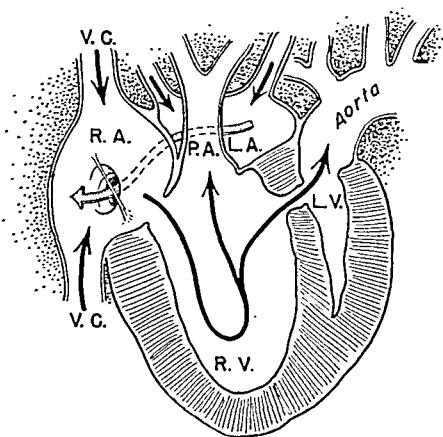


Fig. 19—Diagram of intracardiac circulation in atresia of mitral orifice.

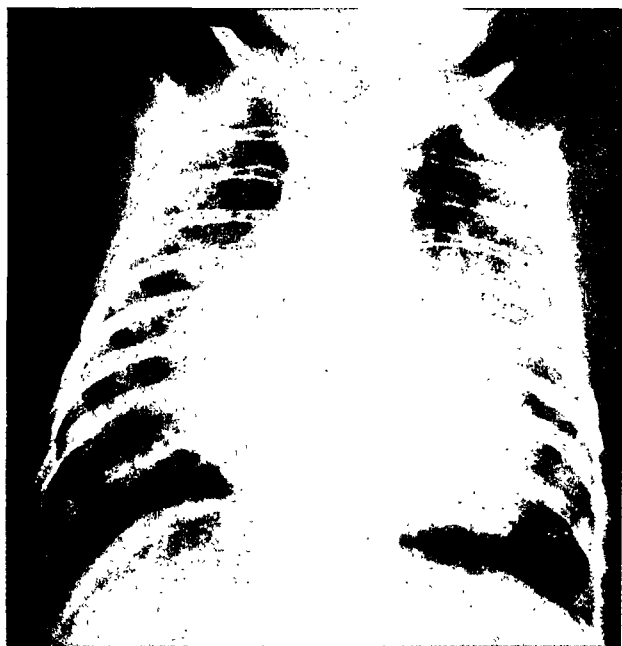
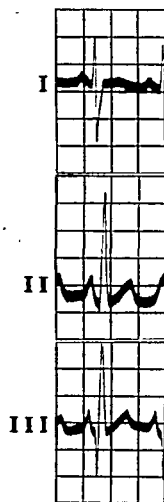


Fig. 20—Electrocardiogram and thoracic roentgenogram of the patient whose heart is illustrated in figures 16, 17, 18 and 19.

Persistent Common Atrioventricular Canal



FRANKLIN PAINE MALL

1862-1917

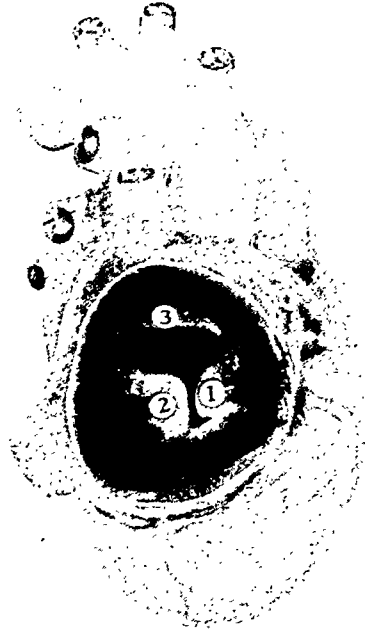
Franklin Paine Mall, professor of anatomy in the Johns Hopkins University Medical School of Baltimore, and director of the Department of Embryology of the Carnegie Institution of Washington, studied structures not simply as morphologic entities but as functioning units. Teacher of teachers, he organized a research institute of embryology. He played a prominent part in the development of many scientific publications. Through the media of these publications valuable information concerning the anatomic nature of cardiac and vascular malformations and a better understanding of the embryologic basis for many of these have been supplied to the profession.

Persistent Common Atrioventricular Canal

IN THIS heart the atrioventricular canal is undivided and is guarded by a single valve composed of a large anterior cusp, a large posterior cusp and smaller lateral cusps. There is a defect in the lower portion of the atrial septum above the common atrioventricular canal.



*Fig. 21—Anterior view (model x1).
(1) Dilated right atrium. (2) Enlarged right ventricle.
(3) Wide pulmonary artery.*



*Fig. 22—Interior of right atrium viewed from above (model x1).
(1) Anterior cusp of common atrioventricular valve.
(2) Posterior cusp of common atrioventricular valve.
(3) Defect in lower portion of atrial septum.*

History of the Patient

FEMALE, 5 months old. Clinical features of mongolism present. Transient cyanosis at birth. Recurrent cyanosis during feeding and crying. Frequent episodes of "choking." Patient admitted with pneumonia. No murmurs heard. Thoracic roentgenogram showed a large globular heart. Lipoid pneumonia was found at necropsy.

Principal Clinical Features of this Anomaly

1. Variable degree of cyanosis (the circulatory abnormality often resembles that in atrial septal defect).
2. Usually systolic murmur over midprecordium and apex.
3. Roentgenologic aspects: right and left ventricle equal in size and both enlarged.
4. Electrocardiogram: usually high voltage biphasic QRS complexes in standard and precordial leads.

Incidence in this Series

Six patients: one stillborn, four patients from 2 to 6 months old and one 36 years old.



Fig. 23—Specimen from which models shown in figures 21 and 22 were prepared. Interior of right atrium and right ventricle.

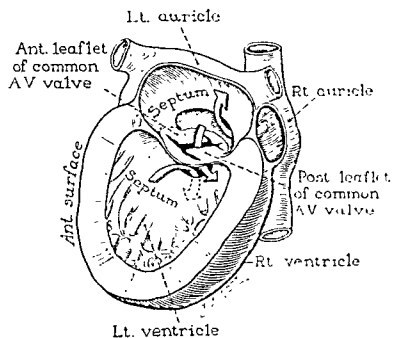


Fig. 24—Diagram of intracardiac circulation in persistent common atrioventricular canal.

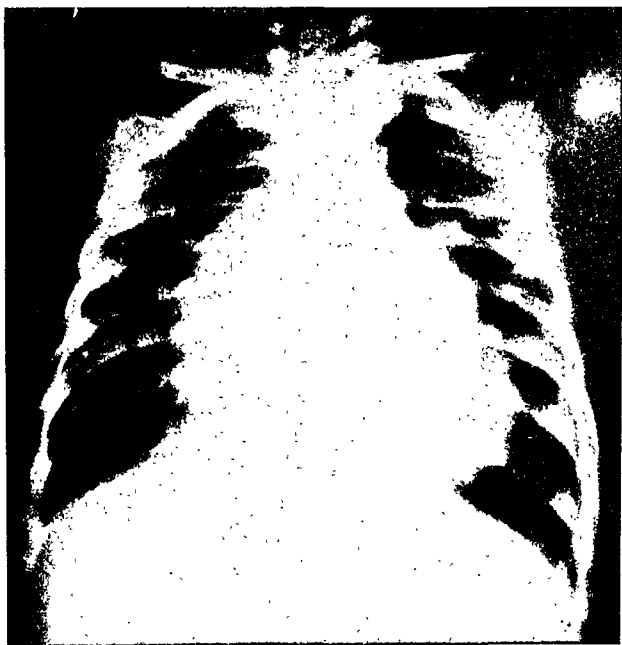


Fig. 25—Thoracic roentgenogram of the patient whose heart is illustrated in figures 21, 22, 23 and 24.

Atrial Septal Defect



JAMES HOPE

1801-1841

That James Hope was the first clinically to diagnose pulmonary stenosis with a venous arterial shunt and to predict the anatomic defects is generally accepted. He closely followed a clinical case, described what he thought would be found post mortem, and was correct (1830). To Julius Friedrich Cohnheim (1839-1884) in 1877 goes the credit for his contribution on paradoxical embolism through a patent foramen ovale.

Atrial Septal Defect

IN THESE two hearts the anomaly is an atrial septal defect in the form of a patent foramen ovale. As a consequence of the left-to-right shunt, there is enlargement of the right atrium and right ventricle and of the pulmonary artery.



Fig. 26—Interior of right atrium viewed from above, model x1.

1. Margin of large defect in atrial septum.
2. Dilated right atrium.



Fig. 27—Heart viewed from right, half-size model.

1. Margin of large defect in atrial septum.
2. Interior of dilated right atrium.
3. Dilated pulmonary artery.
4. Hypertrophied wall of enlarged right ventricle.

History of these Patients

FEMALE, 5 years old (fig. 26). Periodic cyanosis, beginning at 1 year. Pneumonia at 3 years. No murmurs heard at any time. Intermittent auricular flutter. Patient died with congestive heart failure. **Man**, 75 years old (fig. 27). Recurring congestive failure for eleven years. Right hemiplegia at 64 years. Loud precordial systolic murmur. Thoracic roentgenogram (fig. 30) shows tremendous enlargement of heart, and electrocardiogram shows right axis deviation. Patient died with congestive heart failure.

Principal Clinical Features of this Anomaly

1. Characteristically, no cyanosis.
2. Systolic murmur usually present, not diagnostic in type. Accentuated second sound at pulmonary area; occasionally a soft diastolic murmur of pulmonary insufficiency.
3. A major defect may be present for many years without cardiac symptoms. Unexpected sudden death occasionally occurs.
4. Abnormally high oxygen saturation of hemoglobin of blood in right atrium; greatly in-

- creased pulmonary blood flow (cardiac catheterization).
5. Roentgenologic aspects: marked enlargement of atria, right ventricle and pulmonary artery. Accentuated hilar pulsations. Occasionally, aneurysmal dilation of pulmonary artery.
6. Electrocardiogram: right axis deviation. One of the few congenital anomalies in which auricular fibrillation often occurs.

Incidence in this Series—Twenty-seven patients, 10 adults, of whom 12 were over 50 years old.



Fig. 28—Specimen from which the model shown in figure 26 was prepared. Interior of right atrium.



Fig. 29—Specimen from which the model shown in figure 27 was prepared. Interior of the left atrium and mitral valve.

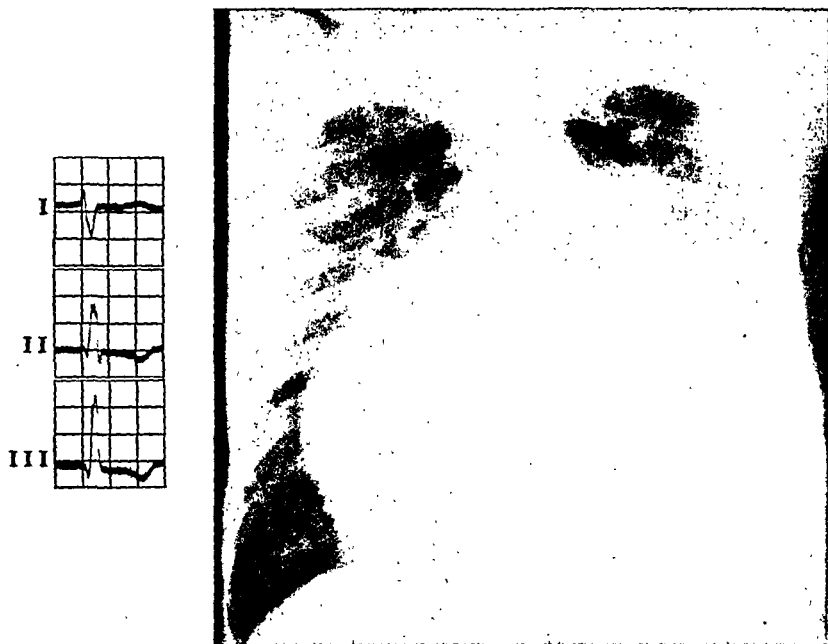


Fig. 30—Electrocardiogram and thoracic roentgenogram of the patient whose heart is illustrated in figures 27 and 29.

Ventricular Septal Defect



HENRI-LOUIS ROGER

1809-1891

Roger demonstrated the presence of a ventricular septal defect, but without stenosis of pulmonary arteries, in a boy who had not been cyanotic during life. Clinical signs in association with an uncomplicated septal defect are so well described that the term "maladie de Roger" came into common usage. He recognized the thrill and described the murmur (bruit de Roger) characteristic of a defect in the ventricular septum.

Ventricular Septal Defect

TWO TYPES of ventricular septal defects are illustrated by these two hearts. In one the defect is in the muscular portion of the ventricular septum. In the other the defect involves the membranous portion. The latter type is the more common.



*Fig. 31—Interior of left ventricle (model x1).
(1) Margin of defect in muscular portion of ventricular septum. (2) Intact membranous ventricular septum.*



*Fig. 32—Interior of left ventricle (half-size model).
(1) Margin of defect in membranous portion of ventricular septum. (2) Wide pulmonary artery. (3) Aortic orifice.*

History of these Patients

A MALE, 5½ months old (fig. 31), had had feeding difficulty since birth, with poor development. A loud systolic murmur was maximal in third left interspace. Dyspnea present for two months. Roentgenogram (fig. 35) shows moderate enlargement of heart. Progressive failure with terminal cyanosis. A woman 54 years old (fig. 32) at 32 years had had a loud, harsh, systolic murmur over entire precordium, accentuated P-2; mild exertional dyspnea, enlarged heart. She was readmitted at 54 years because of fracture of femur. Slight cyanosis and mild congestive heart failure were found. She died of pulmonary embolism.

Principal Clinical Features of this Anomaly

1. Loud systolic murmur (Roger murmur) maximal in third left interspace, associated thrill.
2. No cyanosis (interventricular A-V shunt).
3. High oxygen saturation of hemoglobin of blood in right ventricle as compared to that in hemoglobin of blood in right atrium.
4. High incidence of subacute bacterial endocarditis.
5. Roentgenologic aspects: heart is normal in size and contour in most instances.
6. Electrocardiogram: usually normal (congenital heart block, which is rare, usually occurs with this lesion).

Incidence in this Series—Sixteen patients (6 were 12 years old or more; three were over 54 years old).



Fig. 33—Interior of the left ventricle. Specimen from which the model shown in figure 31 was prepared.



Fig. 34—Interior of the left ventricle. Specimen from which the model shown in figure 32 was prepared.

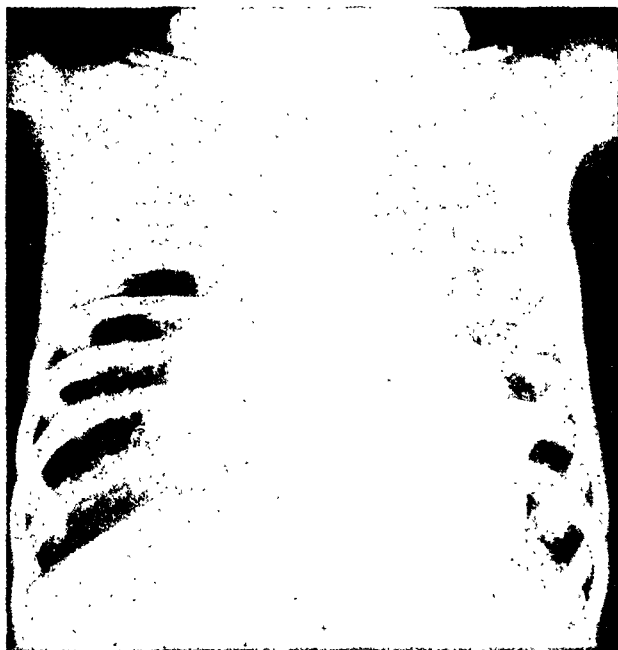


Fig. 35—Thoracic roentgenogram of the patient whose heart is illustrated in figures 31 and 33.

Eisenmenger Complex

(Ventricular Septal Defect with Dextroposition of Aorta)



VICTOR EISENMENGER

1864-1932

Eisenmenger's article appeared in 1897 under the title of "Die angeborenen Defecte der Kammerscheidewand des Herzens." In this article he described a combination of congenital anomalies in which the arrangement is similar to that seen in the tetralogy of Fallot except for the fact that the pulmonary artery, rather than being narrowed, is either normal or dilated.

Eisenmenger Complex

(Ventricular Septal Defect with Dextroposition of Aorta)

IN THIS heart the aorta arises from both ventricles and straddles a defect of the membranous portion of the ventricular septum. The pulmonary artery, arising from the right ventricle, is dilated and has a normal valve. The right ventricular wall is thick.



Fig. 36—Anterior view (model x1).
(1) Dilated pulmonary artery. (2) Aorta.
(3) Large right ventricle.



Fig. 37—Interior of right ventricle (model x1).
(1) Wide pulmonary orifice. (2) Ventricular septal defect below biventricular origin of aorta.

History of the Patient

A MALE, 11 months old, with normal development. One week before his admission cough, fever and cyanosis had developed. Heart sounds obscured by wheezes and rales. Hemoglobin 15.6 gm. per 100 cc.; erythrocytes numbered 5,000,000. Thoracic roentgenogram (fig. 40) showed cardiac enlargement and prominent pulmonary conus and hilar markings, consolidation of upper lobe of right lung. Patient died on day of admission, with extensive bronchopneumonia.

Principal Clinical Features of this Anomaly

1. Cyanosis, often delayed in onset and of increased intensity, with development of polycythemia (oxygen saturation of arterial hemoglobin slightly or moderately decreased).
2. Basal systolic murmur usually present.
3. Pulmonary blood flow not diminished. Pulmonary artery pressure increased (cardiac catheterization).
4. Roentgenologic aspects: right ventricular enlargement and prominent conus shadow.
5. Electrocardiogram: right axis deviation; often large biphasic QRS complexes.

Incidence in this Series—Five patients: ages ranged from 2 months to 47 years.



Fig. 38—Interior of the left ventricle. Specimen from which the models shown in figures 36 and 37 were prepared.

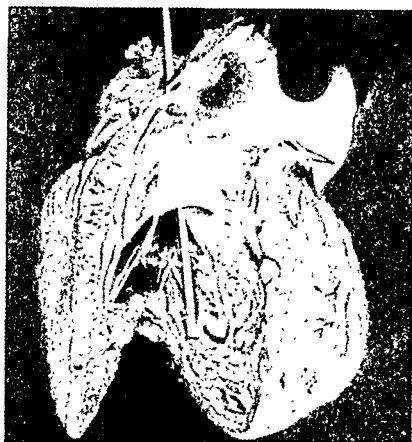


Fig. 39—Interior of the right ventricle. Probe in right ventricle and aorta. Specimen shown in figure 38.



Fig. 40—Thoracic roentgenogram of the patient whose heart is illustrated in figures 36, 37, 38 and 39.



Pioneering in Anesthesiology

RALPH M. WATERS*

MADISON, WISCONSIN

ON A cold, windy day in the winter of 1912-13, a medical practitioner in a small city in our Missouri River Valley turned over to me his office, whatever I could retain of his practice, and his bull terrier. He was bound for Vienna, postgraduate study, and, I suspect, specialization in the future. The office was spacious and "well located" over a drug store. The practice which came to me, largely referred by the pharmacists downstairs, most often proved to be drug addicts seeking relief in those days before the Harrison antinarcotic law. The dog, a very unsatisfactory companion for a bachelor, would not eat in the presence of human observers and caused me much inconvenience. I collected \$1.44 in fees the first month without accepting the largest roll of bills I had ever seen up to that time; it was offered by an addict if I would inject a syringe of cocaine solution into his vein.

One of my duties in conducting the practice was occasionally to administer somnoform (a then popular mixture of ethyl and methyl chloride and ethyl bromide) to the patients of a neighboring dentist. I was permitted to join the informal and unorganized staff of my predecessor's hospital. A surgeon there possessed an apparatus for the administration of nitrous oxide, but no one, except the advertising "painless" dentists, knew how to use this agent. I

volunteered, and thus the foundation for my career of specialization was laid.

In general, the line drawn between specialists and general practitioners was at that time neither very straight nor very distinct. For instance, I am sure that 75 per cent of the members of the county medical society attempted, at least occasionally, to perform major surgical operations. I was not without guilt myself in those days. In a then recognized hospital, I once anesthetized a woman while a man removed her uterus without benefit of ligature or suture. Clamps were applied to the vessels *after* the bleeding had become "less active" and the wound was closed about the clamps. Believe it or not, she lived long enough to regain consciousness. In the good old days a suction tip in the anesthetist's hand often supplemented the skill of the surgeon's dissection of numerous pairs of tonsils.

The requirements for specialization in many mid-western hospitals consisted of the possession of sufficient audacity to attempt a procedure and persuasive power adequate to gain the consent of the patient or his family.

With native intelligence and periodic visits to centers of medical learning in this country and abroad, a creditable specialist often eventually resulted. Techniques were not so intricate nor was the breadth of knowledge so extensive as at present. Frequently a "half-baked" specialist designated him-

*Professor of Anesthesiology, University of Wisconsin Medical School, Madison.

self as paying "special attention to" this or that. A practitioner especially interested in gynecology for instance, had printed on the door of his office and on his professional cards and stationery, "John Doe, M.D., Special Attention to Diseases of Women." The first formal recognition of limitation in my own practice was upon professional cards carrying the notation "Practice Limited to Obstetrics and Anesthesia." This was solely because I liked to do such work and had no thought of the impossible conflicts in appointment that were bound to occur.

After three years of mixed experience and a month's visit with an eastern anesthetist, my practice in the small midwestern city became "limited to anesthesia." I was a specialist. Many a fellow practitioner in the Mississippi Valley and its tributaries became a specialist in similar fashion in the years before the first World War. To be sure, residencies in some of the specialties were available in hospitals associated with the better medical schools. Occasionally a man studied a specialty for several years in European clinics. On their return these men usually settled in the large centers on the seaboard. Some became specialists by associating themselves with an older preceptor in the specialty. In the main, however, specialists as I saw them in the midwest originated as I have described.

Generally, incomes depended more upon the boldness of the man and his economic acumen than upon his professional proficiency. Then, even more than now, the color of a man's necktie, the length of his waistline, his glibness of tongue, or his cheery manner had much to do with his success. I once had the unpleasant duty of anesthetizing a woman for the removal of her kidney by a "surgeon" who had tied off the ureter at a previous simple hysterectomy. When I returned the patient to her room, the husband detained me for some time with a recitation of the virtues and skill of the operator.

FROM what I have said, it should be obvious that financial success and even professional recognition in a specialty could be gained without a great outlay of time and study. It was quite another matter regarding one's own self-respect and personal satisfaction. Within a few months of the beginning of my special interest it became evident to me that

(1) interest in anesthesia was superficial when it existed at all in this country; (2) opportunities for training were scarce; and (3) such contributions as were being made came largely from those whose primary interest was surgical or that of the laboratory. Real specialists in anesthesia were rare indeed.

In certain centers a very few physicians had interested themselves in the practical and technical aspects of the subject. I found that the source of this interest was Great Britain and that the first scientific specialist in anesthesia (I had almost said the only one) began his practice and his investigations almost with the first public demonstration of surgical anesthesia.

It was on October 16, 1846, that Morton first administered ether at Massachusetts General Hospital in Boston. A month later, John Snow began the study and the administration of ether.¹ Dating from January 28, 1847, he reported that "the ether produced the desired effect in every operation performed in St. George's Hospital." Snow's biographer says, "What had been a mere accidental discovery, I had almost said a lucky adventure, was turned by the touch of the master [Snow] into a veritable science." Although Snow died eleven years later, his influence remained. His scientific study and application explains much of our present knowledge and skill at the end of the first century in the use of anesthesia. The respect in which Snow was held by the profession in Great Britain influenced high-caliber men throughout the British Empire to follow in his footsteps. The few men such as Bennett, Gwathmey, and others who specialized in anesthesia in this country received their inspiration not from New England but from Snow and his followers in Great Britain. To this day, in the British Empire, the administration of anesthetic agents has never been entrusted to those who do not have a medical degree.

I have written elsewhere of the influence of publications and organizations upon the development of this specialty during the present century.² Others will record the influence of the recent war. My own effort has been along lines of undergraduate and graduate teaching and investigation; in other words the contribution of the medical school. After ten years of private practice "limited to anesthesia," two things seemed obvious to me. First, improve-

ments in our knowledge of the subject, the whys and hows of both the science and the art, depended upon close cooperation of those who administered drugs in the operating room with those who worked in the laboratories. Only in the medical school can such cooperation be established. Second, so long as the majority of physicians had little or no understanding of the dangers, the importance, and the possible contributions to the welfare of patients which anesthesiology can offer, no improvement or recognition could be expected. Again the medical school was the answer. Only when every medical college is teaching those whom it graduates the real foundations upon which sane administration of narcotic drugs must be based, can we expect the profession to appreciate and demand legitimate service for its patients.

In early days the deplorable belief was common, and still lingers in the minds of some of the profession, that the best in anesthesia lay in the "choice of agent," the selection of a particular drug with some occult fitness for administration in a given case. Little consideration was given to the all-important fact that all known anesthetic drugs and methods of using them often produce dangerous side effects. We were long in recognizing that it is the anticipation and recognition of these undesirable physiologic disturbances accompanying anesthesia and their management and control which constitute wise and safe anesthesia.

IN 1927, I was glad to accept a place on the medical faculty at Wisconsin. Objectives of that position from the beginning have been fourfold. In order of their importance they still remain: (1) to provide the best possible service to patients of the institution; (2) to teach what is known of the principles of anesthesiology to all candidates for the medical degree; (3) to help long-term graduate students not only to gain a fundamental knowledge of the subject and to master the art of administration, but also to learn as much as possible of effective methods of teaching; and (4) to accompany these efforts with the encouragement of as much cooperative investigation as is consistent with achieving the first three objectives.

Some of the details of our attempts to carry out

these objectives have been published in previous papers.^{3,4,5,6} It will be sufficient to say here that we believe our undergraduates have acquired only what is essential by a didactic period once a week during the second half of their third year (junior) and a service of two weeks in the operating room during their senior year. This we feel gives only the minimum of information and experience in anesthesiology necessary for any well-informed physician. If anesthesiology as a specialty is contemplated, a residency of at least three years' duration seems to be advisable. To review our experiences and personal conclusions regarding these residencies at Wisconsin after twenty years may be of interest to others. Some of the conclusions apply to the specialty of anesthesiology only. Others seem to me of general application to graduate instruction in all the specialties.

Possibly by accident, and certainly for selfish reasons at first, resident graduate students in the specialty were chosen who had had some experience in anesthesia as a special interest during a period of general practice. Compared with individuals who come right to specialization from a rotating internship, such residents seemed to have definite advantages. It has been my practice, almost without exception, to urge, if not require, that every applicant for an appointment on our service finish a period of two or three years in general practice before he makes a final decision as to what specialty he desires to enter.

After observing individuals for twenty years, both during their training period and following it, I feel quite sure that an interval in general practice before specialization is highly desirable. I believe that the younger doctor who follows the plan of internship, general practice, final decision as to his specialty, and then a long-term residency will be more successful and more satisfied ten years after graduation than would the same individual if he went into a specialty directly following his internship. This statement, I realize, demands some defense.

From the young man's standpoint it may be argued that a period of general practice before specialization delays the beginning of one's real life work until the individual is too old for real enthusiasm. Economic security may be delayed, and the early establishment of a family and a permanent

home of one's own may be impossible. However, as I look back upon those who have been associated with me in the study of anesthesiology in the long past, these two objections seem to be overbalanced by numerous advantages. At least some of these men who became specialists married, had families, and yet were economically stable and happy.

THE hospital staff and management may argue that the resident with previous experience in general practice is intractable, less cooperative, less studious, and more demanding. Some of these objections depend upon the point of view. If, as a primary function, the hospital expects its residents in the specialties to care for its patients, and to do the work of the hospital and the visiting staff, then the younger and less experienced in life they are, the better. For instance, I know of hospitals that have "modernized" their service in my own specialty by replacing former technicians in anesthesia—the so-called "anesthetic nurses" who got a salary of \$150 or more a month—with "residents" in anesthesia, young doctors at 25 dollars a month. These "residents" have been allowed to anesthetize patients, private and others, without proper supervision or instruction while the hospital budget is balanced by the fees which it collects for their services.

If, as I believe, residencies or fellowships in the specialties are maintained primarily for the purpose of creating capable specialists who will contribute the maximum in efficient service to the public in the future, it is the responsibility of the hospital to provide time, opportunity, and instructors necessary to prepare them. An immature youngster just finishing his internship may be happy with the opportunity to care for patients independently, to operate upon them, or to anesthetize them, and to permit such experience to be called "training for a specialty." The man with experience in general practice does not accept such conditions as "graduate training for a specialty." We, as staff members and hospital administrators, must guard against having opinions or supporting practices which contribute to the convenience of the visiting staff and the economic security of the hospital at the expense of the quality of special training offered. I am suggesting that the maturity of the man who begins to special-

ize after a brief experience in general practice will prevent us—teachers, visiting staff, and hospital administrators—from exploiting, however unconsciously, the graduate student.

But, you say, common honesty and understanding on our part will prevent exploitation of the graduate student. Agreed. What then are the real advantages of the plan I am proposing? They extend in two directions—to the community and to the young doctor. One of our unsolved problems in recent years has been the deficiency of available family practitioners to serve our smaller communities. If every medical graduate, on finishing his internship, were to undertake a short period of general practice, this shortage would not exist. A few months or years of such experience gives the young doctor an opportunity to learn how to collect and spend money, how to conduct himself in his relations with the community in which he lives, with patients and their families, and with other physicians. It is so easy to acquire a critical and unsympathetic attitude in a specialty. It is less easy when one has lived "on the other side of the fence." But more especially the young doctor during general experience will see all sides of the practice of medicine; he will refer cases to specialists; he will learn that no patient is the problem of a single specialty. While making these observations, he will be in a position to decide just what specialty he will really enjoy and where his inclinations and skills will fit.

What about the community when he leaves to begin his special residency or his fellowship? Once the custom becomes established, will not a heritage develop much as it operates now regarding internships? Certain schools establish the custom of sending a man to this hospital, another to that, each year. As long as the hospital is satisfied, the habit continues. Sometimes it is a fraternity or some other small group which determines what hospital a particular senior will choose for his internship. Would not the same habit develop in determining where he would enter general practice the next year? The office, equipment, even the motor car and living quarters, might be handed down in a similar manner. If, as I am sure would happen, an occasional young doctor decided that he likes general practice and did not return for training in a specialty, I believe both the community and the pro-

fession would benefit by the doctor's decision.

To implement such a plan as I am advocating, a slight change is necessary in customs among administrators. Interns have said to me, "I like the idea of having experience in general practice before I decide what specialty I shall enter. But I get the impression that it will be next to impossible for me to secure a desirable appointment in a first-class department unless I arrange for it while I am an intern." Obviously, if the intern waits to avail himself of experience and maturity before choosing his life work, he must not be penalized for it. If more mature individuals are appointed, it is my firm conviction that the hospital superintendent and the director of training in any specialty will observe benefit not only to the graduate student but also to the service.

Even when a person has the advantage of a period of general practice during which he decides upon a specialty, he may be mistaken regarding his preference. Actual experience may prove that his aptitudes lie elsewhere. Both the candidate and our department always look upon the first six months of a resident's service as a trial period. If either side decides that a mistake has been made, we try to rectify it as soon as possible. Although these methods of deliberation in planning one's future may seem like waste of time, they make for satisfaction and success in later life. Everyone is not intrinsically equipped to be a surgeon, an obstetrician, an internist, or an anesthetist. May it not be advantageous to spend a reasonable time in deliberation and experimentation? Certainly there should be no disgrace attached to changing one's mind about the choice of his future life work. If the choice has been right, life is a joy forever after. Uncongenial work is drudgery.

What does the evidence show in the later experience of our own men who have gone out as specialists in anesthesiology? I am quite willing to admit that the number has been altogether too small to have the slightest statistical significance. We have had with us residents of three categories: (1) those who came to the specialty from their internships; (2) those who have had an interval of two or three years in general practice; and (3) a few who have come to us late in life, sometimes after part-time specialization for some years. What can we say of

their comparative accomplishments?

Those in the first group acquire knowledge and technical facility as readily as the others. On the other hand, as a group while in residency they show less good judgment, less independence of thought, and less self-reliance. They are more, rather than less, likely to give evidence of brashness or foolhardy conduct. After leaving us, when "out on their own," the first group have had more difficulty in building a place for themselves in the world. Their relations with hospital staff or medical school faculty, with hospital administrators, and with the community at large, have been more difficult at first and satisfactory adjustments have been made much more slowly.

THE second group, who have returned after an experience of two or three years in general practice, have, in our experience, shown little or no tendency to resist the necessary routine of a department, record-keeping, cooperation, and the like. They have adjusted to institutional life without difficulty. As a group, they offer more original ideas, good and bad, which not only prove a healthy stimulus to discussion in the department and to investigative effort, but also at times result in change of conviction in the department. The advantage to us and to our institution deriving from this second group over the first, though noticeable, may not have been great. The advantages to the resident himself, however, both during his training and in later life, seem to us considerable. He comes to us after a mature choice of what he wants to do. He works harder and grasps his opportunities with more vigor. Possibly the fact that he is older and more mature when he begins to practice "on his own" explains some of his advantage. However, I do not believe that age and maturity are the only factors. The broad viewpoint acquired as a general practitioner remains with him as a specialist. Experience in economic and social relations does not have to be acquired at a time when he is trying to establish himself as a specialist.

Finally, what of those in the third category who have been out in the world for a good many years either as part-time specialists or as general practitioners? Some of these are merely men who,

through failing health, deficient professional background, or desire for change, wish to specialize. These must be discouraged at once. An old dog doesn't learn new tricks very easily. As a rule, those in the third class do not fit into a residency program nor do they benefit themselves thereby. We have met a few exceptions to the rule, but these are rare indeed.

Personal acquaintance with candidates through long correspondence and at least one protracted personal interview is necessary if the director of a training program is to fulfill all his obligations. These extend not only to the applicant but to the applicant's prospective fellow students, to the specialty and last, but most important of all, to the medical profession as a whole and the service it will render to the public. If we cannot help young physicians to become specialists who will be a credit to our profession, if we do not put them in a position to perform a useful service in years to come, our efforts had better not be devoted to the "training of specialists."

SUMMARY

Specialization in medical practice has developed as knowledge and skills have extended with the years. Methods of preparation of specialists have varied widely. I have related some personal experiences and observations both as student and as teacher. The very informal customs I have described as being characteristic of some parts of our mid-west at the time I began practice in 1893 had certain advantages. Independence, self-reliance, and originality were developed; or at least these qualities, when naturally present, were not diminished. Sometimes, however, the freedom allowed led to boldness, rashness, and foolhardy practice, resulting, in certain cases, in disaster and death, if not murder.

Certainly it was not the ideal manner of preparation. We have speculated as to how the advantages of the informal, individualistic method of learning to be a specialist can be combined with the advantages of the formal training that is customary at the present time.

I think we may conclude that familiarity with physiologic functions and the manner in which these are altered by therapeutic procedure is the essential background of specialization. Added to such familiarity, technical skills in diagnosis and treatment are not enough to produce a real specialist. He must also have a rational, well-rounded attitude toward the general problems involved in the practice of medicine and the care of the sick. If our training of specialists sacrifices one of these three factors, either scientific background, special skills, or a rational, well-rounded attitude, it is not very successful.

Having tried to select those candidates for special training in anesthesiology who have acquired a general practice after internship and having watched a fairly large number of these later as specialists, in comparison with others who began to specialize directly after internship, I cannot avoid certain definite impressions.

1. The former general practitioners are happier and are better satisfied with their specialty.
2. They are more successful and more satisfying professionally as specialists.
3. They more easily and completely command the respect and the economic recognition of fellow physicians, hospital administrators, and the public.

It is my belief that a young person will act for his own and the communities' best interest if he delays decision as to specialization and his choice of a specialty until he has passed through at least a short period in the general practice of medicine or its equivalent.

REFERENCES

1. WARREN, R. M.: John Snow, first anesthesiologist. *Proc. Soc. Med.*, March, 1937.
2. ———: The development of anesthesiology in the United States. *J. Journal of the History of Medicine and Allied Sciences*, Vol. I, No. 4, 1946.
3. ———: The teaching value of records. *J. Indiana M. A. Assoc.*, March, 1937.
4. WARREN, R. M., HARRINGTON, H. R., and CLEGG, W. B.: The relation of anesthesiology to medical education. *J.A.M.A.*, 1940, April 20, 1941.
5. WARREN, R. M.: The evolution of anesthesia. *Proc. Staff Meet. Mayo Clin.*, 1940, No. 27, July 25, 1940.
6. ———: Anesthesiology in the hospital and in the medical school. *J.A.M.A.*, 1939, April 20, 1940.

The Medical Bookman

THE DIGESTIVE TRACT IN ROENTGENOLOGY, by Jacob Buckstein, M.D., Assistant Professor of Clinical Medicine, Cornell University Medical College; Visiting Roentgenologist (Alimentary Tract Division) Bellevue Hospital, New York City; Attending Gastroenterologist, Beth David Hospital, New York City; Consultant in Gastro-Enterology, Central Islip State Hospital, New York. 889 pages with 1030 illustrations, including 659 figures. Philadelphia, J. B. Lippincott Company, 1948. Price \$16.00.

For more than twenty-five years, Jacob Buckstein has made roentgenologic examinations of the digestive system in Bellevue and other New York hospitals. From his assiduously correlated his observations and opinions with clinical, operative and postmortem data. This extensive and comprehensive experience, augmented by that of a large private practice, he has described and explained normal and abnormal conditions of the alimentary tract and ancillary organs. The expository text is supplemented by abundant and pertinent case records.

The sections on the small intestine contain important material, and the plates of ascariasis and hookworm are unusual. Roentgenologic consideration of the appendix is also uncommon, but sensible and satisfactory.

The numerous illustrations aptly identify the material discussed, but many of the reproductions are slightly dim and blurred, probably because of having been used in the author's other publications. The chapter in general the references are not up to date, but do list original articles of historical interest. The chapter on gastritis in particular is incomplete, and does not include recent data.

The opinion of the value of properly interpreted observations of the progress meal for study of colon function is conservative, and justly assigns significance to this procedure. Several usually neglected subjects such as valvulus of the sigmoid and eventration of the diaphragm are adequately mentioned.

The emphasis given normal appearance and insignificant abnormalities of the alimentary tract and accessory organs is gratifying and should instruct inexperienced radiologists. The historical backgrounds introductory to the major subjects are interesting.

TREATMENT OF HEART DISEASE. By William A. Brams, M.S., M.D., Ph.D., Associate Professor of Medicine, Northwestern University Medical School, and Attending Physician, Michael Reese Hospital, Chicago. 195 pages, with 11 figures. New, 1st Edition. 1948. W. B. Saunders Company, Philadelphia & London. Price \$3.50.

This book comprises a systematic and practical guide in the treatment of heart disease, based on the author's own experience in private and hospital practice. Dr. Brams has devoted space to discussion of such important coexisting conditions, as diabetes, thyrotoxicosis, pregnancy, etc., as they relate to the treatment of heart disease. He also stresses the ability to treat congestive heart failure as an essential prerequisite for successful treatment of heart disease.

MODERN CLINICAL PSYCHIATRY. By Arthur P. Noyes, M.D., Superintendent, Norristown State Hospital, Norristown, Pa. 525 pages. 3rd Edition. 1948. W. B. Saunders Company, Philadelphia & London. Price \$6.00.

This book has been re-written to state more fully and clearly the genesis, dynamics, and manifestations of personality functioning incident to dealing with the anxieties and frustrations attendant to the task of living. The author believes that any concept which deals with personality functions must take into consideration the integrated facts of biology—atomic, physiologic, chemical, and psychologic. He has attempted, therefore, to construct these concepts of personality functioning in psychobiologic terms, that is, in terms of total integration of the organism.

A HISTORY OF THE HEART AND THE CIRCULATION. By Frederick A. Willius, M.D., M.S. in Med., Senior Consultant in Cardiology, Mayo Clinic; Professor of Medicine, Mayo Foundation for University of Minnesota; and Research, Graduate School, University of Minnesota; and Thomas J. Dry, M.A., M.B., Ch.B., M.S. in Med., Consultant, Section on Cardiology, Mayo Clinic; Associate Professor of Medicine, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota. 456 pages, illustrated. 1948. W. B. Saunders Company, Philadelphia & London. Price \$8.00.

J. B. C.

Dr. Donald C. Balfour, who recently retired from his position as Director of the Mayo Foundation for Medical Education and Research, says in the preface to this book: "In a systematic approach toward any project to advance knowledge in a field it is axiomatic that intimate knowledge and understanding of the historical data pertaining to the field are essential. . . . This is particularly true in the field of cardiology, for of all the diseases which afflict mankind, heart disease occupies a place of ever-increasing importance among the medical specialties."

HANDBOOK OF TREATMENT and Medical Formulary. By Charles M. Gruber, Ph.D., M.D., Professor of Pharmacology, Jefferson Medical College, Philadelphia. 585 pages. 1948, F. A. Davis Company, Philadelphia. Price \$7.00.

This book has been designed to present in condensed form the essentials of modern treatment for practically every disease the clinician may be called upon to handle. Under each alphabetically listed disease are explicit directions on care and management, selected prescriptions, and differential diagnosis where helpful. The nearly 1,500 selected prescriptions include the most recent information on the use of therapeutic agents and procedures, as well as the older remedies that have been proved efficacious and rational.

PERIPHERAL VASCULAR DISEASES, Diagnosis and Treatment. By David W. Kramer, M.D., F.A.C.P., Associate Professor of Medicine, Jefferson Medical College. Foreword by Edward L. Bortz, M.D. 620 pages, 157 illustrations with 25 in color. 1948, F. A. Davis Company, Philadelphia. Price \$8.00.

As Dr. Edward L. Bortz says in the foreword of Dr. Kramer's book, "Disturbances of the peripheral vascular system represent a large group of important problems and. . . . Here is a volume that squarely meets the needs of the modern practitioner. One finds here a clear description of the important diseases which is of value in appraising the efficiency of the peripheral circulation. Points of differential diagnosis have been accentuated. Significance of newer therapeutic procedures and agents has been stressed, and detailed instructions for their use are given."

PRACTICAL BACTERIOLOGY, HEMATOLOGY AND PARASITOLOGY, by E. R. Stitt, M.D., Ph.M., Sc.D., LL.D., Rear Admiral, Medical Corps, Surgeon, U.S. Navy, Rtd.; Paul W. Clough, M.D., Physician-in-Charge of Diagnostic Clinic, Johns Hopkins Hospital; and Sara E. Branham, M.D., Ph.D., Sc.D., Senior Bacteriologist, National Institute of Health. 10th Edition, 991 pages,

765 illustrations. Philadelphia: The Blakiston Company, 1948. Price \$10.00.

This edition, prepared with the collaboration of specialists in the various fields, presents all types of laboratory procedures, including clinical chemistry. Emphasis has been placed on the practical details of technic, guidance in the selection of approved methods, and interpretation of findings. The book is divided into four main sections under the headings of: (1) Bacteriology, (2) Hematology, (3) Parasitology, and (4) Clinical and Pathologic Examinations of Body Fluids and Organs.

HEMOSTATIC AGENTS. By Walter H. Seegers, M.S., Ph.D., Professor of Physiology, Wayne University College of Medicine, Detroit; and Elwood A. Sharp, M.D., Sc.D., Director, Department of Clinical Investigation, Parke, Davis and Company; Lecturer, Department of Medicine, Wayne University College of Medicine, Detroit. 131 pages, with 27 illustrations, some in color. 1948, Charles C Thomas, Springfield, Ill. Price \$4.75.

Based on developments during the past few years, this monograph is intended to cover the subject of coagulants and their clinical utility. A summary of blood coagulation mechanisms has been included by the authors to consolidate scattered information and as orientation for the successful use of modern hemostatic agents in surgical practice.

CONTROL OF PAIN WITH SADDLE BLOCK AND HIGHER SPINAL ANESTHESIA. Edited by J. H. Walton, M.D., with illustrations by Frank H. Netter, M.D. 52 pages, including 12 color plates. Summit, New Jersey: Ciba Pharmaceutical Products, Inc., 1948.

CORONARY HEART DISEASE. By A. Carlton Ernstene, M.D., Chief of the Section on Cardiovascular Disease, Cleveland Clinic, Cleveland, Ohio. 102 pages. 1948, Charles C Thomas, Springfield, Ill. Price \$2.50.

This monograph is an excellent summary of the subject of coronary heart disease. The author describes the principal clinical manifestations of the disease such as angina pectoris, acute myocardial infarction, acute coronary failure, paroxysmal dyspnea, auriculoventricular and intraventricular block, other disturbances of cardiac rhythm, and congestive heart failure.

Recent advances in methods of diagnosis and treatment are discussed and the subject is brought up to date in all ways.

The book is written in a clear and concise style and should prove a valuable addition to the library of everyone interested in the subject of coronary heart disease.

T. Z.



EDITORIALS



GASTRIC CANCER

FIFTY YEARS ago, only one gastric cancer in every 100 was resectable. Today, of those patients treated in medical centers, one in every 3 or 4 is reported as resectable. But this fact, however suggestive of surgical progress, has only academic interest, for it reveals but a small segment of the truth. A recent survey of deaths from "cancer of the stomach" in a representative metropolitan area demonstrated that two-thirds of the victims never entered a hospital. Less than 6 per cent were given the benefit of gastric resection. Obviously, therefore, if this survey reflects the true community picture, operative mortality could be reduced to zero, and still 94 per cent of all gastric cancer patients would die of the disease.

Real improvement in the cure-rate, therefore, depends upon those persons who first see the patient, and whose responsibility it is to make the diagnosis and get the patient to surgery. These men include the family doctor, the diagnostician, and the roentgenologist. If these physicians fail in their diagnosis, or if they delay in getting the patient to surgery, no amount of surgical skill will save him. But if they render an accurate diagnosis, and provide surgical treatment prior to lymph node involvement, then the patient has at least a 50-50 chance to live five years.

The medical treatment of gastric carcinoma leads only to death. Consequently, all gastric ulcers should be regarded as malignant until they are proved otherwise. One investigator has graded stomach ulcers in terms of coins. Those ulcers larger than a silver dollar he regards as almost certainly malignant. Of all lesions be-

tween the size of a quarter and that of a dollar, one half are carcinoma. Since this crude diagnostic formula is just about as accurate as anything else short of surgery, the physician might do well to manage a small gastric ulcer of doubtful malignancy as follows: a careful, accurate and aggressive medical trial may be allowed for a period not to exceed two or three weeks. If the ulcer does not heal within that time, the final test should be made to determine its true nature. This requires a surgical exploration; the ulcer should be biopsied, and its nature determined while the abdomen is still open. The mortality rate from this operation should be less than one per cent. Continued medical management of a malignant ulcer yields a 100 per cent mortality rate.

Improvement in survival rates from gastric cancer depends almost entirely upon earlier diagnosis of gastric lesions. Several new techniques are now being studied, which undoubtedly will lead to more accurate diagnoses. At the present time, however, relatively few diagnosticians are competent in the use of these techniques. As time goes on, this condition should improve. Biopsy with the aid of the gastroscope is still being experimented with; it is a promising technic. Skillfully employed, the fluoroscope yields diagnoses of gastric lesions which are accurate in about 95 per cent of cases. Perhaps the most interesting diagnostic development is the use of the Papanicolaou technic in detecting exfoliated malignant epithelial cells in the gastric contents. This may prove to be the "screening test" that so many have been hopeful of developing. Fluoroscopic examination of large unselected groups of people offers little encouragement, but such an exam-

ination of those brought into focus by gastric analysis and Papanicolaou test smears would be quite feasible. There can be little doubt that as these improved technics of diagnosis become more widely used, gastric cancer will become a less fatal disease.

Today, operations are being successfully performed which, prior to the development of anesthesiology and chemotherapeutics, would have been impossible. Total gastric resection is now being performed with fairly acceptable mortality figures while only ten years ago few series claimed less than 50 per cent. More frequent removal of the total stomach is being recommended for smaller lesions. It is possible that the principles stated by Halstead for radical removal of cancer of the breast may well be adopted for cancer of the stomach. Gastric resection, however, must not be considered a casual operation; nor should it be performed by a casual surgeon.

From 40,000 to 50,000 gastric carcinomas appear annually in the United States. From the best criteria available for comparison only 10,000 of these are to be considered resectable when first seen. Further, it is estimated that at least 10,000 persons die every year from gastric cancers that are still in resectable stages. These large numbers illustrate what an enormous gap exists between our present, available knowledge and our functional use of it in this disease. Small percentage gains in cure of cancer of the stomach have just as great practical significance as a far greater percentage gain from the cure of malignancies in other organs where the occurrence is of lower incidence in the population. A 2 to 5 per cent increase in the cures of cancer of the stomach means a salvage of more lives than from the 100 per cent cure of all cancers of the lip that occur in one year.

R. L. C.

DOCTORS OF HAPPINESS AND HEALTH

AMERICANS are traditionally jealous of their rights to life, liberty, and the pursuit of happiness. To these, some would also add

the right to health, to be guaranteed by law. Whether or not the government ever could guarantee health, depends, of course, upon whether one concedes that it is possible to legislate people into being healthy. Past experience of other countries who have tried this venture seems to prove conclusively that it cannot be done. Perhaps more could be accomplished if the people and their physicians concentrated more on the third of the freedom triad, the pursuit of happiness. For therein, it seems apparent, lies an important key to health. Traditionally, people strive to be healthy in order to be happy. Isn't it even more important to strive for happiness, in order to obtain health?

The recent progress in psychosomatic medicine has shown that emotional calmness, an indispensable prerequisite to happiness, is also necessary for physical health. Every doctor has patients who manage to be quite happy, although very unhealthy, sometimes being hopeless invalids. But who can remember many who were chronically unhappy over a very long period of time without being ill, often physically as well as mentally? Recognition of the emotional tension of unhappiness is not too difficult, once the search is begun. And the search does yield dividends, once the physician seeking a diagnosis takes the trouble to make it. Dr. Walter Alvarez sums this up in a foreword to *Brief Psychotherapy* by Bertrand F. Frohman, M.D. (Lea & Febiger):

"Actually, because of the way he is trained at college, if an able young assistant were to see his chief diagnose a neurosis at a glance or after a few searching questions, and then see him start treatment without going on to take all the patient's spare cash for a complete overhauling, I think he, the assistant, would be upset; he would feel that his chief was too old-fashioned and unscientific to be trustworthy."

Doctors need no longer be ashamed of this type of acumen, which, unfortunately, few possess. The old family doctor often had it, but on the other hand he often used vague generalities to cover an appalling ignorance of the rapid strides that scientific medicine was mak-

ing. Were he practicing today, he would be equally far behind in the field of psychosomatic medicine, for it, too, has become a science. The old family practitioner was close enough to his patients to recognize their unhappiness and when subsequently it resulted in poor health, he was in the way of expecting it. The doctor of today is rarely on such intimate terms with his patients, so we need very badly to learn ways of discovering unhappiness in our patients, scientific ways, if we must have science, willy-nilly. Actually, there are such scientific ways which can easily be learned by every doctor and should be ingrained into the young physician while he is learning his trade. Medi-

cal science can relieve the pain of an ulcer through diet, medication, or even cutting the vagus nerve, but who takes the trouble to see that the chronic unhappiness that largely caused the ulcer in the first place has been cured? There lies *real* preventive medicine.

If, as physicians, we are custodians of the health of those we serve, then we are equally the custodians of their happiness, and it behooves us to inquire into ways of uncovering emotional discontent and relieving it. Only then will we be practicing the real idealistic medicine to which we are dedicated, and perhaps earn the accolade given to Luke, "The Beloved Physician."

F. G. S.

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New Drugs and Instruments

Information published in this department has been supplied by the manufacturers of the products described.

VI-LITRON WITH FOLIC ACID

PURPOSE: Prevention and treatment of many forms of anemia.

COMPOSITION: Each VI-LITRON capsule contains:

Liver concentrate*	218 gm.
Ferrous sulphate	3 gr.
Ascorbic acid (C)	20 mg.
Folic acid	2 mg.
Thiamine (B ₁)	2 mg.
Riboflavin (B ₂)	2 mg.
Niacinamide	10 mg.
d-calcium pantothenate	1 mg.

*Anti-secondary anemia fraction derived from 12 gm. of liver.

DOSAGE AND ADMINISTRATION: 3 to 6 capsules daily or as needed.

HOW SUPPLIED: VI-LITRON with FOLIC ACID: in packages of 48, 96, 200, and 600 capsules.

PRODUCER: U. S. Vitamin Corporation, New York, N. Y.

ENTEROGASTRONE HYDROCHLORIDE

PURPOSE: Symptomatic relief of peptic ulcers.

COMPOSITION: A sterile, lyophilized extract of the upper portion of the small intestine of hogs, containing principles that inhibit gastric secretion and protect gastric and duodenal mucosa from ulceration.

INDICATIONS FOR USE: For providing relief of symptoms of peptic ulcers usually within a few days, and healing within two to five months after initiation of treatment.

DOSAGE AND ADMINISTRATION: Daily dose is 200 mg. dissolved in 4 to 5 cc. of sterile water, given intramuscularly only. Injections are made daily except Sunday for a period of one year.

CAUTIONS: Intradermal sensitivity tests should be made prior to use, particularly in patients with history of allergy.

HOW SUPPLIED: Package containing 200 mg. enterogastrone hydrochloride in a 10 cc. vial, and one 5 cc. ampule sterile water.

PRODUCER: The Upjohn Company, Kalamazoo 99, Mich.

PENICILLIN DULCET TABLETS

PURPOSE: They are designed especially for children.

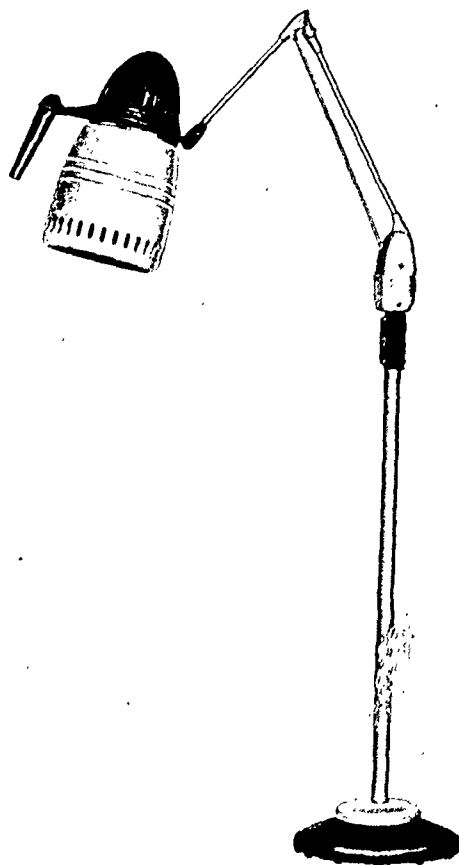
DESCRIPTION: They are like candies in appearance, taste, and odor, yet are accurately standardized medication. Each white, cinnamon-flavored, buffered tablet provides 50,000 units of crystalline penicillin G sodium.

INDICATIONS FOR USE: The same as those for other oral penicillin preparations.

ADMINISTRATION AND DOSAGE: The same as for other oral penicillin preparations.

HOW SUPPLIED: Penicillin *Dulcet* Tablets (Buffered), 50,000 units, are supplied in bottles of 12.

PRODUCER: Abbott Laboratories, North Chicago, Ill.



DAZOR SUN-HEAT LAMP FIXTURE

DESCRIPTION: The Dazor Sun-Heat Lamp Fixture is of the pedestal-type having a circular cast iron base. Above the base is an upright bearing the switch box and the pivot for the floating arm bracket. The reflector housing at the far end of the outer arm contains a plastic heat-resistant handle for positioning. The fixture is especially useful in connection with RS sun bulbs drawing 275 watts on 110 to 125 volts alternating current and R-40 heat bulbs drawing 250 watts on 110 to 125 volts alternating or direct current. The diameter of the base is about 30 cm. (12 inches), and the whole weighs 11.3 kg. (24 $\frac{7}{8}$ pounds); the shipping weight is 17 kg. (37 $\frac{1}{2}$ pounds).

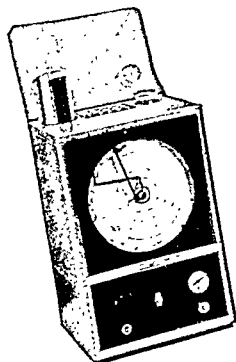
PRODUCER: Dazor Manufacturing Corp., St. Louis, Mo.

VIDEROL

PURPOSE: For treatment of arthritis and associated fibrositis.

COMPOSITION: Each capsule contains:

NEW DRUGS AND INSTRUMENTS



KIDDE UTERO-TUBAL INSUFFLATOR

The Kidde Tubal Insufflator offers the gynecologist a safe, simple means of carbon dioxide gas tubal insufflation. A weighted piston called the Gasometer has been injected in the carbon dioxide line between the high pressure source and the outlet to the patient so that there is no possibility of introducing a pressure surge into the patient because of the unyielding gravity control. The Kidde unit is not dependent upon the function or nonfunction of valves. It is supplied with either the direct recording Kymograph or Mercurial Manometer pressure recorder.

At a slight additional cost, the Kidde Opaque Oil attachment which holds the opaque medium delivers this medium to the patient under the automatic and positive pressure control of the gasometer in the Kidde Tubal Insufflator.

PRODUCER: Kidde Manufacturing Co., Inc., Bloomfield, N.J.

ACNOMEL

PURPOSE: For effective acne therapy.

INDICATIONS: Resorcinol, 2 per cent; sulfur, 8 per cent; in a stable, grease-free, pleasantly scented, flesh-tinted vehicle.

DESCRIPTION: Acnomel is entirely free from wax, oil, or other greasy substance, is a cosmetically superior treatment for acne and rosacea.

INDICATIONS FOR USE: Acne vulgaris and acne rosacea.

CAUTIONS: Should not be applied to diffuse, acutely inflamed areas. Use with care near the eyes. In blonde and dry-skinned persons, the erythema and scaling which are normal and expected results of the application of Acnomel may become too marked. If this occurs, its use should be discontinued until inflammation has subsided, and, thereafter, should be applied at longer intervals.

HOW SUPPLIED: In 1½ ounce tubes, specially lined to preserve the quality, since Acnomel is designed to dry quickly when applied.

PRODUCER: Smith, Kline & French Laboratories, Philadelphia 5, Pa.

BIOGELS

PURPOSE: Multivitamin capsules for diet supplementation.

COMPOSITION:

	In each Biogels capsule 500 USP units	Minimum adult daily requirement 4,000 USP units 400 USP units
Vitamin A		
Vitamin D		
Vitamin B ₁ (thiamin hydro- chloride)	3.0 mg.	1.0 mg.
Vitamin B ₂ (G) (ribo- flavin)	3.0 mg.	2.0 mg.
Vitamin C (ascorbic acid)	100.0 mg. 50.0 mg.	30.0 mg. Not established; 12 to 23 mg. recommended by National Research Council
Nicotinamide		
Calcium pan- tothenate	5.0 mg.	Not established
Vitamin B ₆ (pyridox- ine)	.05 mg.	Not established
Vitamin E (mixed tocopher- ols)	5.0 mg.	Not established

POSAGE: One Biogels capsule supplies more than the minimum daily requirements of vitamins A, B₁, B₂, C, and D for prophylactic purposes, with a generous margin of safety.

HOW SUPPLIED: Bottles of 100 soft gelatin capsules, specially designed to facilitate swallowing.

PRODUCER: Bristol Laboratories, Inc., Syracuse, N.Y.

Vitamin D (as viosterol)
Mixed Tocopherols

30,000 units
50 mg.
150 mg.

Desical (whole bile) (2½ gr.)
INDICATIONS FOR USE: Chronic arthritis and conditions associated with primary fibrositis.

DOSAGE AND ADMINISTRATION: Best results are obtained when Capsules Viderol are administered in maximum tolerated doses. For the average patient the following dosage schedule will usually be satisfactory: initially, 1 capsule three times daily for three days, then increased every third day by 1 capsule until 6 capsules are taken daily. This dosage should be continued until improvement is obtained and then gradually reduced. Since effective doses vary for each individual, it is important that the patient be kept under close observation and dosage adjusted according to response. If toxic manifestations such as nausea, vomiting, frequency of urination, or nocturia are encountered at any dosage level, Viderol therapy should be discontinued for one week, then resumed and increased gradually until a maximum of 6 capsules are being administered daily. If toxic manifestations recur, high vitamin D therapy should be discontinued.

HOW SUPPLIED: Bottles of 100 and 500 capsules.

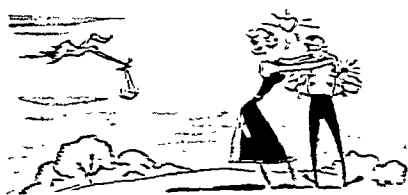
PRODUCER: Parke, Davis & Company, Detroit 32, Mich.

Leaves from a Doctor's Diary

By MAURICE CHIDECKEL

August 1 . . . Spoke colleague Burt: "The human animal, not unlike all living matter, is subject to unpredictable changes which we scientists call mutation."

The fibroma of bachelor maiden Elizabeth, for example. That fibroma. It constitutes a poignant record of a unique experience, both intellectual and emotional. The virgin sat and listened to specialist Eddington as he learnedly delivered for her his dissertation on uterine tumors, of the malignant that break down their barriers and of the benign; of the submucous, the interstitial, and the peritoneal. Her tumor is what "we gynecologists" call encapsulated "and I shall shell it out of its bed like that." He snapped his fingers as an illustration of his skill.



But the female wizard took sick and Elizabeth would have no one else. Hence she waited. But the tumor would not stay put. One dark night the maiden felt pain and as it grew in intensity I was summoned. What a strange apparition of a neoplasm, for I could hear a heart beating into it. Pain and more pain, a burst of fluid and out came the tumor shrieking and kicking. Bewilderment, shock and doubt as a little girl of seven pounds was placed alongside of her. "How did

that thing ever get into me?" she asked and shrugged her shoulders. No, no. The audacity of my inquiries. No man ever dared any familiarity with her. "Take that creature away," she commanded.

Before dawn that fine baby was in the house of a childless, cultured couple. That was one year ago today. The mother instinct must have awakened of a sudden in the virgin mother. She was leaving town and she wants that baby "you found in my bed." But that good couple have long ago left for California where they now reside. "Have another baby," I advised her. "How?" she thundered. "Use the same method you employed in the first one." I heartily recommended. Her lips quivered. "So you still believe that I indulged in—" As she took a pitcher from the table to transmit it to my head I thought best to retire.

And there is Solomon Wise who is not wise at all, for he is rocking a baby and thinks he is rocking his own. When told that she was pregnant three months, Margaret married Wise the same day. She suddenly became so lonely for him, and she loved him so. Of course it was a premature baby. The fact that it weighed eight and a half pounds is beside the point. And Sol is so happy that the baby did not have to be put in an incubator. Yes, I know who the father is. Sol isn't.

* * *

August 4 . . . Dr. Lanimer is the peripatetic protagonist of Communism. He must help rescue the world from folly, he must help to

destroy the menacing tentacles that reach out towards all men in present day bourgeois society, which, so says the learned man, is of the lowest moral and spiritual stagnation. To be a Communist one must also be an Atheist.

A very successful and very competent cardiologist, the doctor teaches and preaches the Utopian realization of a new order. I stood near him as he sat beside the patient with congestive heart failure. He spoke interestingly of the value of circulation time, vital capacity tests, weight and venous pressure measurements as compared to evaluating the signs and symptoms manifested by the patient.

"Is he better?" tremblingly inquired the patient's wife. The doctor nodded in the affirmative. With folded hands and upraised eyes the wife exclaimed: "Oh, I thank Thee, Lord in Heaven." The learned man regarded her disdainfully. "Some day," he addressed himself to me, "there will be complete daisy in religious belief. With the increased comprehension of the elements and of evolution the narcotic called religion will become extinct. Tell me why does the Lord deserve thanks because this man is better. I do. And I didn't make him sick." He placed his arms akimbo and paced the room. "Primitive man found explanation in malign spirits and he would bribe and outwit those spirits. Now man pleads, promises and lies to something unseen and unknown. Why should man's journey through life be determined by something that I know does not exist. In the days when religion dominated mankind, man suffered from the cruellest despotism."

And now, doctor? In the countries where religion has become extinct and Communism reigns over the bodies and souls of men, does not the imagination falter before the spectacle of cruelty? Does not the excuse of harsh necessity reduce man in those lands to the level of a robot? And why, doctor, should you be a fanatic of a more-

LEAVES FROM A DOCTOR'S DIARY

ment, and yet condemn fanaticism, even pure belief in a Supreme Being? Life is always extraordinarily well adjusted to the kind of world one lives in. Wouldn't you benefit humanity much more by concentrating your fine mind on your work?

I indulged in one of my hobbies—listening. I went outside and leaned against the wall of the hospital. The fog was thick and the night an inky blackness. I heard a woman's voice: "I am afraid. It's so dark." The man: "But I am with you." The woman: "That's why I am afraid. Yes, yes, I know you. That makes it worse." She ran into the corridor of the hospital. A strikingly attractive girl.

Soon I recognized the voices of eccentric philosophy teacher Walden and that of his wife. Evidently they were robbed in the darkness. The couple forms a fine example of marital disenchantment. She calls him *The Last Illusion*. From him: "A strange, ungrateful creature, that's what you are. Aren't you thankful this was the first time we were ever held up? Aren't you going to offer up thanks that the thugs took our money and spared our lives? Aren't you overjoyed that we had that much money and no more, and aren't you—" "Dry up," she commanded. And there was silence all around.

August 10 . . . There were the classic symptoms of intracranial pressure due to brain tumor located in the posterior fossa in a little girl of nine. There were present the characteristic papilledema, occipital headache radiating to the neck, and vomiting. Visual acuity was not changed. She was admitted to hospital because of convulsions. Neurosurgeon Walter operated on her. I don't know why mental symptoms of intellectual deterioration, confusion, memory impairment, dullness, and loss of initiative began after the operation. Dr. Walter is being sued for a huge sum.

The complaint states the child became mentally unbalanced because of the operation.

The lawyer for the plaintiff began to implant into the minds of the jury the conviction that the girl never needed an operation, and that she was used as an experiment.

With a few typed pages before him the lawyer spoke with such dispassionate serenity, his words were delivered with such pace, verve and drama, full of color and interest that the neurosurgeon almost began to believe it himself. Of a sudden the legal genius flung the typed pages aside, and as he began to speak extemporaneously he converted himself into the typical jackass. He turned on all taps and began to denounce the medical profession. He called all doctors, and especially brain surgeons "nuts" and then tried to be funny. "We should be thankful to the doctors. They kill us today, so we won't have to die tomorrow. Yes. They bury their mistakes. But here is one mistake they could not hide."

He suddenly noticed me among the audience. "Gentlemen of this jury," he screamed, "look at this doctor." He pointed at me. "Look at him. Last week my intimate friend Frank Gould had a slight case of indigestion. He sent for this doctor. When he left, Frank was dead."

As I became the center of attention and as a few necks were craned to look at the killer I walked out, accompanied by a few hisses. And who faced me in the corridor? Mrs. Gould. "I was at your office to sign these here blanks for that there insurance company. They told me you were here. Damn it. I have so much trouble with these here insurance blanks that I am beginning to be sorry that Frank is dead." At the present writing the case still goes on.

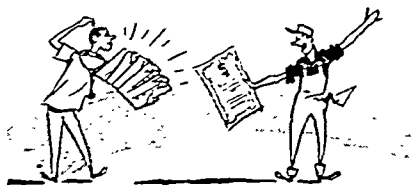
August 13 . . . From soft spoken, dignified Mr. Gassner: "You know my father-in-law. Yes, you do, the one who works in that storage plant.

Well, his doctor told him that he suffers from chronic poisoning of carbon dioxide. That doctor says that my father-in-law is exposed to sublethal doses of that stuff. Now what is sublethal? Oh, I see, almost fatal—"look. Do you know a whisper—making it real fatal? He is heavily insured. There is plenty in it for you—"

August 18 . . . Fatal. Dr. Coates was visibly unhappy and very much confused. His patient became wildly excitable and uncontrollable as the doctor was removing the esophagoscope. A few minutes later his patient was dead. The doctor addressed himself to the patient's wife, forgetting that he was talking to an unlettered laywoman. "You see, the ending was fatal. He may have developed mediastinal emphysema, and the result was a rupture of the mediastinal pleura. Whether the pneumothorax was secondary to perforation of the piriform sinus or was spontaneous is hard to tell." "Is that good?" she asked indifferently, "thanks, doc." "Madam," the doctor spoke agitatedly, "I said his case ended fatally." "Fatally, smartly, so it ain't dangerous." She was in a happy mood, and as someone called me by name she turned quickly. "Oh, so you are that doctor? I thought you looked different." I said, "Did you imagine me short and ugly?" She laughed. "No, I thought you were tall and handsome."

August 23 . . . As I practice. Spoke elderly Dr. Boles: "Efforts to prevent conception are widespread." His young wife interrupted: "You certainly need no efforts to prevent it, do you, dear." The word "dear" was uttered way the word "dear." A type is still ringing in my ears. Dr. Boles is still himself this good Dr. Boles. He comes to the clinic daily but each morning he interrupts the work with some new joke. Just where he picks them up I don't

know. Today's joke was: "Hey, men, does any one of you know the difference between crime and prostitution? No? Well, crime does not pay."



Received five expensive shirts, half a dozen costly neckties and a tie clasp from bricklayer James Harcourt whom I have never seen. His uncle recently died of pulmonary embolism. "Dear Doctor," said the note, "you made me the happiest man in the world. My uncle made me beneficiary in his twenty thousand dollar policy. Gosh. You did a quick job. Thanks again."

Samuel Samuelson's gastric ulcer followed a second degree burn—not at all an uncommon occurrence. "Your ulcer came from your

burns," I told him. "You mean from your salve you gave me for those burns. No, no. I don't want to sue you, unless I have to. I just hate court suits, and I hate juries. What's a jury? Just men to decide who has the better lawyer. I'll tell you what. Let's settle it out of court. Just give me a paltry five thousand and we'll forget the whole business. Just five thousand. That's all." "That's all," piped his wife.

Two colleagues. Two cases of chickenpox next door to each other. Both patients developed auriculo-ventricular block. One doctor is accused of having caused the trouble by the medicine he gave (penicillin); the other because he gave none.

Elderly, unattractive, pimply, thick-lipped Mrs. Chades, with protruding yellow teeth and odor not so sweet, suffering from dysphagia, refuses to go to the gastroenterologist I referred her to because his wife is away and she trusts no doctor though he is very good on the stomach. "Those stomach specialists, they all make love to me." Poor specialists.



August 30 . . . Such is the practice of medicine. The woven fabric of my dreams of the long ago when I just started out are dull alongside the vivid color of actuality. Then I didn't know there is such a host of enigmas and cheats and men of offensive, insupportable arrogance. Sometimes I find man hard to understand. Sometimes the world and events look to me like a somnambulist procession. No one knows whither or why. Yet my faith in the dignity of men was never lost. There is always a taper of light in dense darkness; and while there are beastly creatures in human form, the vast majority of men and women are humane, good and honest, and some of them even pay their medical bills. What else can one ask?

INTERNATIONAL ASSEMBLY

Public Auditorium

Cleveland, Ohio

November 9 to 12, inclusive, 1948

Thirty-third Year



Foreign Bodies in Air and Food Passages

CHEVALIER L. JACKSON*

TEMPLE UNIVERSITY SCHOOL OF MEDICINE, PHILADELPHIA

MY SUBJECT is "Foreign Bodies in the Air and Food Passages," but first I would like to make a few introductory remarks with regard to bronchoscopy and esophagoscopy and broncho-esophagology as it is today.

Peroral endoscopy was developed primarily by otolaryngologists for the removal of foreign bodies. Today special training in these procedures, and in "broncho-esophagology" properly constitutes a part of the education of the thoracic surgeon, the phthisiologist, the anesthesiologist, and the gastroenterologist. Bronchial obstruction, its mechanisms and effects, has come to be understood largely through experience with foreign bodies, the ones opaque to the x-ray first, and then the nonopaque ones.

The diagnostic importance of the wheeze indicative of a by-pass valve obstruction, of obstructive emphysema due to a check valve type of obstruction, and obstructive atelectasis due to a stop valve type of obstruction, have come to be generally recognized, and these evidences of bronchial obstruction always call for diagnostic bronchoscopy.

*Professor of Laryngology and Broncho-esophagology, Temple University School of Medicine, Philadelphia.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

Bronchial obstruction is an etiologic and perpetuating factor in postoperative atelectasis, in pulmonary abscess, bronchiectasis, and empyema. Bronchoscopy affords the means of its early and accurate diagnosis, as well as, very often, the means of its prevention or cure.

Signs of bronchial obstruction constitute the earliest manifestations of bronchial cancer, and early bronchoscopic biopsy conduces to cure by means of early resection. Benign tumors can be diagnosed and removed by means of the bronchoscope.

Modern diagnosis of diseases of the esophagus and stomach is dependent very largely on esophagoscopy and gastroscopy, and the gastroenterologist of today must master the technic of peroral endoscopy. Largely through experience with bronchoscopy and esophagoscopy for foreign bodies, broncho-esophagology has developed as a new branch of medicine, and knowledge of it is essential in the training of the internist, the thoracic surgeon, the phthisiologist, the anesthesiologist and gastroenterologist, as well as the otolaryngologist.

Though the work with foreign bodies these days constitutes a small percentage of the work of any broncho-esophagologist, it still is a vitally important and certainly a very interesting part of his work.

ETIOLOGY

Study of the etiology of foreign bodies has shown us that carelessness of one kind or another is the cause in almost 90 per cent of the cases—carelessness in the preparation of food, carelessness in eating, carelessness in looking after infants and young children.

Age is an important etiologic factor because 80 per cent of patients with foreign bodies are under 15 years of age. Artificial dentures are important in two ways: first, because they may occur as foreign bodies themselves when not properly adjusted; and secondly, they are an important etiologic factor in the swallowing of foreign bodies such as bones or chips of china or other foreign material in food that is not detected in the mouth because the patient wears a denture which prevents the foreign body from being felt as it otherwise would be.

Coughing, laughing, crying, vomiting, and fainting are all contributory factors in these accidents. Dental and surgical accidents have accounted for a few, resulting in the inhalation or swallowing of some dental or surgical instrument. And finally, insanity or attempted suicide has been a factor in a few cases.

PROPHYLAXIS

We can prevent many of these accidents by more care: (1) more care in the preparation of food and instruction of those who have charge of the preparation of food in observation of reasonable precaution; (2) care in the mastication of food, especially by those who wear artificial dentures; (3) care in the training of children not to put inedible objects in the mouth, which is perhaps easier to advise than to carry out, but nevertheless one can try, and care not to give peanuts or peanut candy to babies under 2 years of age who cannot chew; finally, avoidance of setting a bad example to children by putting inedible objects in one's own mouth, and (4) care on the part of dentists and surgeons who work about the mouth not to allow small objects to be inhaled or swallowed.

SYMPTOMATOLOGY AND DIAGNOSIS

THE initial symptoms of a foreign body accident, regardless of where the foreign body eventually lodges, are choking, gagging, coughing, wheezing, and very important, as has been pointed out a number of times before, is the *symptomless interval* that generally follows these initial symptoms.

The localizing symptoms, if the foreign body is in the *larynx*, may be hoarseness, croupy cough, dysphonia, wheezing, dyspnea and cyanosis in the case of obstructive objects.

In *tracheal* foreign bodies the principal symptoms are an asthmatoïd wheeze, cough, or a slapping sound produced by a freely moving tracheal foreign body.

Bronchial foreign bodies produce cough, blood-streaked sputum, and wheezing in many cases. If they are nonobstructive, however, they may give few or no symptoms for a long period of time. If the foreign body is obstructive, a wheeze is generally noted, and, depending upon the degree of obstruction, the physical and x-ray signs of obstructive emphysema and atelectasis. Vegetable foreign bodies give rise to violent inflammatory reaction in children, with fever and very often croupy cough due to the subglottic swelling, and slightly less severe reaction in adults.

Esophageal foreign bodies may give a subjective sensation of the lodgment of the foreign body, or give difficulty in swallowing, pain in swallowing, sticking sensation, or may give very slight symptoms. In the case of gastric foreign bodies there are generally no symptoms at all.

To summarize diagnosis, *laryngeal* foreign bodies are diagnosed by x-ray studies and by the examination of the larynx with the mirror or the direct laryngoscope, or both. In the case of children one cannot see the larynx with the mirror, so the direct laryngoscope must be used for the laryngoscopic examination.

In *tracheal* foreign bodies the diagnosis is made on the basis of the typical symptoms mentioned above and x-ray examination, which should always be done whether or not the sus-



pected foreign body is opaque to the x-ray.

In *bronchial* foreign bodies, a careful history is important as the first step in diagnosis. Physical signs often present conclusive evidence of the presence of a foreign body. Percussion and auscultation are of the greatest value in demonstrating bronchial obstruction. The roentgen ray is the most valuable diagnostic means whether or not the foreign body is radiopaque, but the roentgen ray may be negative and the physical signs positive. The roentgen examination should include all the structures from nasopharynx to the tuberosities of the ischia. A lateral roentgenogram should never be omitted, and neither should the preliminary fluoroscopic examination. If possible, films should be taken both on full inspiration and full expiration, because in this way only is a graphic record made of the typical appearances of obstructive atelectasis and obstructive emphysema.

In *esophageal* foreign bodies the diagnosis is made chiefly by the roentgen ray with the use of an opaque mixture if the foreign body is nonopaque. The diagnosis of a nonopaque foreign body in the stomach cannot be made by any method except examination with the flexible gastroscope. Opaque foreign bodies, of course, are diagnosed by the x-ray.

TREATMENT

FIFTY years ago, though some surgeons had reported very skillful operations for the removal of foreign bodies, in general the mortality rate was very high, probably as high as 75 per cent. Today the removal of foreign bodies from the air or food passages is carried out by means of the direct laryngoscope, the bronchoscope, or the esophagoscope, and the mortality should be less than one per cent. Endoscopic removal of foreign bodies requires study of the mechanical problem presented in the particular case.

Bones are the commonest objects occurring as foreign bodies. That is not surprising when we think how commonly they occur in food, but the incidence of bones as foreign bodies

can be very much reduced if the public is warned of the risk of this accident.

Most of the little *spicules of bone* occur in the lower pole of the tonsils and the base of the tongue or in the valleculae, but the other bones lodge down in the cervical esophagus. One of the commonest bones is the *triangular part of the sternum of the chicken*.

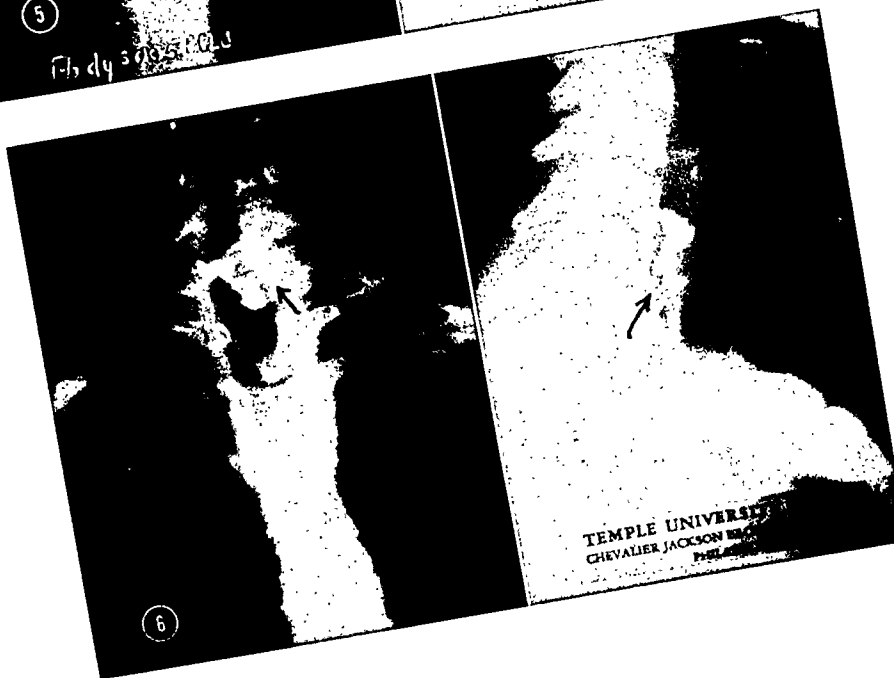
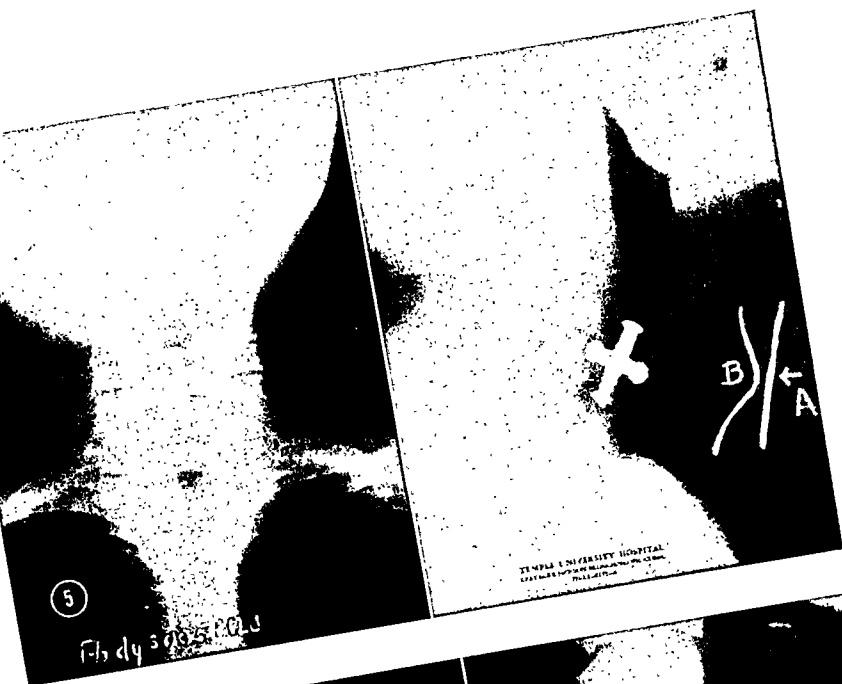
A good x-ray, one taken with the proper technic, will almost always show conclusively a bone in the esophagus. Some years ago x-rays were not that good and we could not depend on them as much as we do now. Almost any bone now will show in the x-ray. The diagnosis in some cases is a little more difficult even with the x-ray showing the bone, because there may be confusion with the ossification in the laryngeal cartilage. Figure 1 shows a bone lodged right behind the cricoid cartilage, but it is a foreign body and not the ossification in the cricoid.

Another common foreign body is a *coin* lodging in the cervical esophagus as shown in Figure 2.

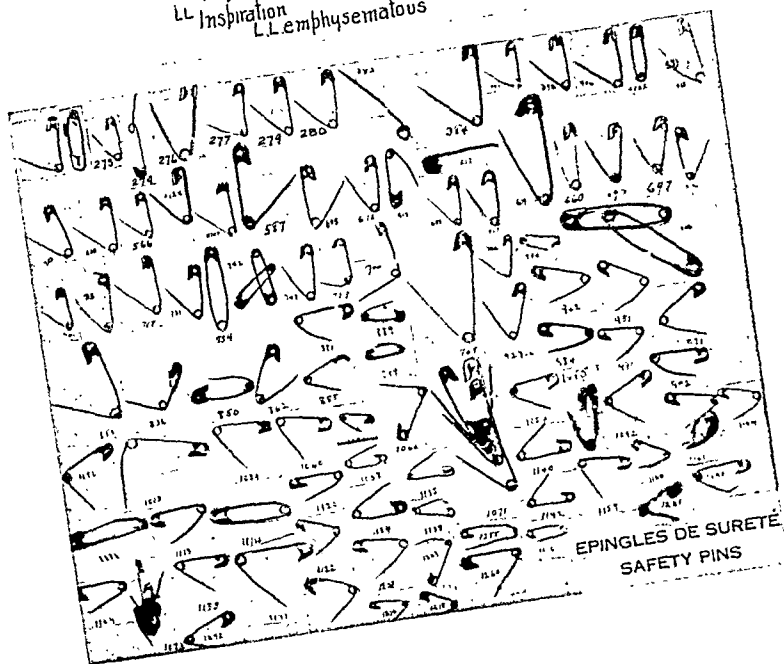
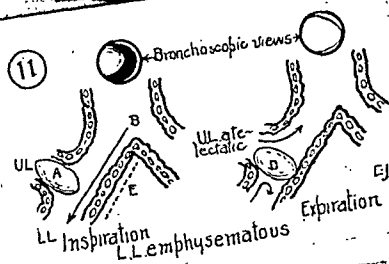
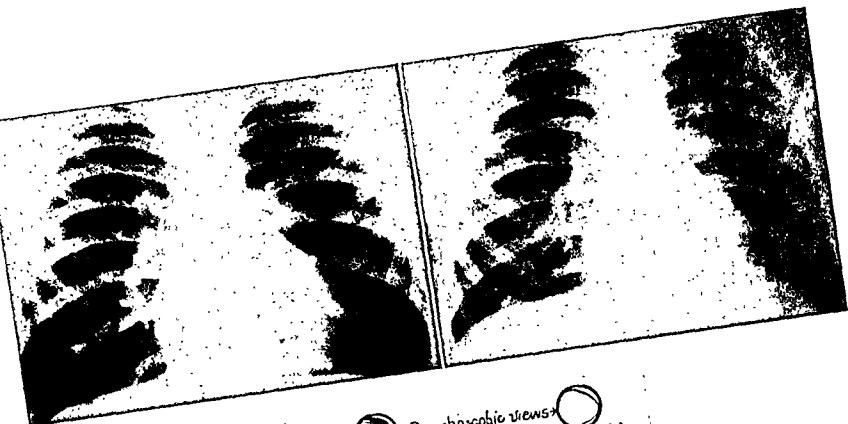
Buttons are likewise quite common and lodge at the same place, and some are nonopaque and are not shown unless one gives a little opaque mixture, which will outline the bone (Figure 3).

It is important for every one of you, I think, to consider this problem at least from one angle, at least from the angle of avoidance of overlooking foreign bodies, because even today with all the literature that has been accumulated about foreign bodies, there are still too many cases of foreign bodies that come to us a week, two weeks, two months, even years after the accident.

Speaking of overlooked foreign bodies, Figure 4 is the x-ray of a girl who came from near Philadelphia. She was thought, as a child, to have choked on a wooden button but it did not cause too much trouble and the incident was more or less forgotten. She grew up, got married, and went to Panama with her husband. A month or two after she got to Panama she was having so much difficulty in swallowing that the doctors made some x-rays. They did







not know just what was wrong but they were sure there was some trouble in the cervical esophagus. They sent her back to Philadelphia and we found that the button was still there. That was one of the cases of longest duration that I know of with this kind of object. It is very unusual for a foreign body to remain so long in the esophagus.

The *jackstones* used as toys are a surprisingly common object, and they cause a lot of obstruction of the airway as well as the esophagus, sometimes sufficient obstruction to necessitate tracheotomy (Figure 5).

A tooth plate, which is just one example of a rather small partial denture, is illustrated in Figure 6.

While we are on the subject of dental objects, you see that there is a great variety to the objects of more or less dental character—teeth and fillings and caps; but these small objects generally occur in the bronchus, sometimes getting quite far peripherally. The root canal reamers, when they go down into the bronchial tree, generally go far out into the smaller bronchi, and they are among the objects that have to be removed with fluoroscopic aid.

THIS very important group of vegetable foreign bodies, peanuts, other nut kernels, seeds, and shells, are especially important in children. One of the large groups of foreign bodies occurring in children is constituted by peanuts and similar nuts, generally in children under 2 years of age. Sometimes we are asked what use there is in taking an x-ray picture in a peanut case, since a peanut will not show up in the film. The point is that though the peanut itself does not show, the effect on aeration does show, and in the fluoroscope and x-ray film you will find either an atelectasis or an emphysema. In this case you have an atelectasis of the left lung due to complete obstruction of the left bronchus (Figure 7).

At the right is the picture after uncorking of the bronchus by removal of the foreign body when perfect aeration has been restored.

In Figure 8 the atelectasis present is also due

to a foreign body, but it is only the right lower lobe that is affected. Either one lobe or the whole lung may be involved.

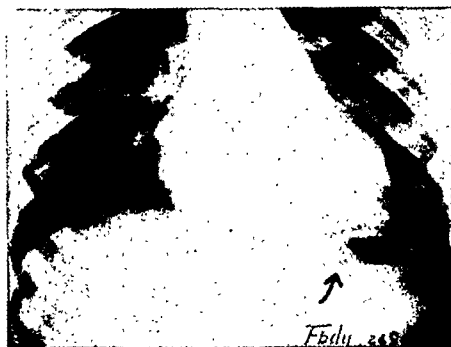
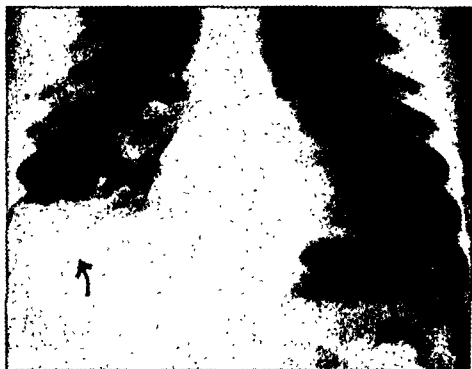
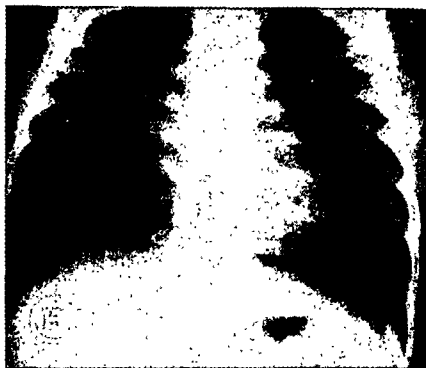
A case of obstructive emphysema is shown in Figure 9. Notice that the right lung is found to be ballooned on expiration. Check valve obstruction of the right bronchus has caused an emphysema. Figure 10 is a case which was one of the difficult ones from the point of view of diagnosis because there was bilateral obstructive emphysema and, in fact, the x-rays were at first reported negative. It was then realized that there was limitation of diaphragmatic excursion and the explanation was that there was bilateral foreign body obstruction—peanuts in both bronchi. (Inspiration film to left, expiration to right.)

A diagram of one of the complicated mechanisms that we find occasionally in some of these cases may be seen in Figure 11. This patient had a prune stone in the upper lobe bronchus. There was alternate atelectasis and emphysema of the upper lobe because it was pumped empty as the foreign body went back into the main bronchus. This could be seen under the fluoroscope and the explanation was determined later by the bronchial examination.

Safety pins constitute a very large and dangerous group of foreign bodies, occurring singly for the most part, and for the most part open. If they are closed, they of course do not involve any particular mechanical problem of extraction and very little risk. They occur sometimes in bunches as in two cases illustrated (Figure 12).

Sometimes the problem of removing a safety pin is very difficult. I will not go into any detail concerning the mechanical problems involved, but there are about seventeen different methods of dealing with an open safety pin. The one in the lower esophagus would probably be best removed by grasping it by the ring and passing it into the stomach, allowing it to turn around, then bringing it out with the point trailing (the method of "endogastric version"). (See Figure 13.)

Figure 14 illustrates a case that is more easily done under biplane fluoroscopic guidance, as



are most cases of screws and nail heads upward in the bronchus. This is another difficult mechanical problem because it is difficult to get the expansion necessary to permit the forceps blades to pass over the head of the screw or nail and extract it. That is more easily accomplished under fluoroscopic guidance.

Screws and nails are often found corroded from long sojourn in the bronchus. Common pins are frequently found and they are also difficult because they go far out into the smaller branches of the bronchial tree and must be removed by fluoroscopic guidance (Figure 15).

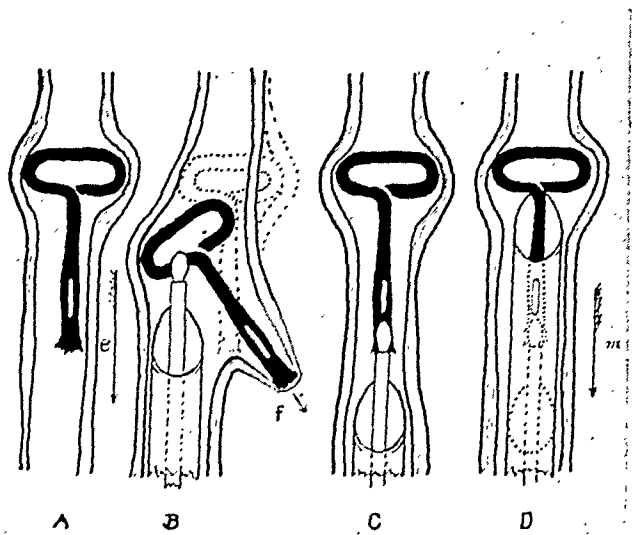
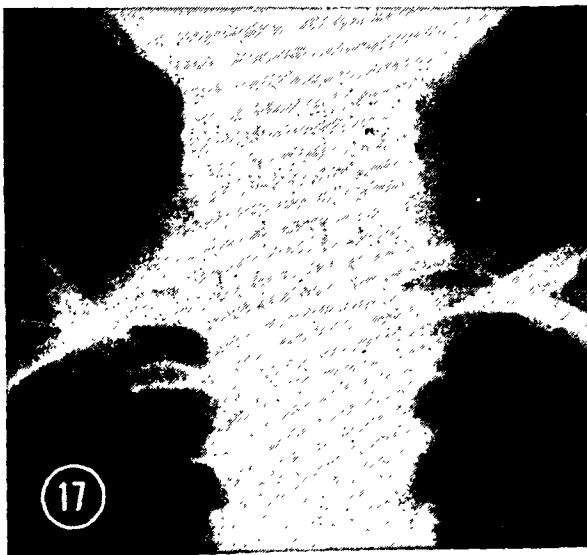
Figure 16 is just one example of a complicated staple case. This man was fixing a fence and had his mouth full of staples and nails when somebody told him a funny story. He got one staple in each bronchus and a nail in the right lower lobe. They were all removed by fluoroscopic guidance. Incidentally he did not realize that he had swallowed the objects until some days after the accident. He went to the doctor a week or so later and said he had a bad cough. I think he mentioned the incident, and the doctor had the x-ray taken, which gave the explanation.

We have had a number of cases in which can openers were swallowed by children (Figure 17). They generally present a mechanical problem. We cannot grasp a foreign body by



the first part we see. If we do, we perforate the wall. We must retreat it down and grasp it by the proper part, removing it without pulling the point into the wall. "Advancing points perforate, trailing points do not."

Meat occurs not infrequently as a foreign body, but generally in patients who have some form of obstruction of the esophagus. It is rarely that meat occurs as a foreign body in the normal esophagus, but occasionally in case of a very hasty and gluttonous eater a piece of meat may stick.





Dissecting Aneurysm of Aorta

JAMES E. PAULLIN¹ AND DAVID F. JAMES²

EMORY UNIVERSITY SCHOOL OF MEDICINE, ATLANTA

FOR THE past ten or fifteen years, we have been interested in the early diagnosis of dissecting aneurysm of the aorta. In 1937 McGeachy and Paullin¹ reported from the medical service of Grady Hospital 6 patients with this disease in whom the diagnosis was correctly made in 3. In 1943, Logue² from our clinic reported 12 patients in whom a correct diagnosis was made in 10. Now, we wish to report an additional group of 11 patients who entered the Grady Hospital from January 1946 to June 1947. Nine of these were correctly diagnosed. Two of these diagnosed as having dissecting aneurysm are living. One of these was operated on by Dr. Osler Abbott and is living at present.

Since 1937, quite a few articles have appeared dealing with this disease. A number of statistical studies have been made detailing the symptoms, physical signs, laboratory findings, and other phases of this symptom complex with which you are familiar.

The purpose of our presentation is not so much to review all of the symptoms, physical

findings, laboratory data, x-ray, and electrocardiographic findings with which you are familiar, but to present a few observations which are of interest in their relationship to the x-ray diagnosis and to the development of methods of treatment.

To briefly summarize our knowledge: It is well known that dissecting aneurysm of the aorta occurs most frequently in men between the ages of 40 and 60 years. The onset is sudden, usually with intense pain which is retrosternal and frequently felt in the back. It may radiate to the arm or to the neck. The pain may begin during exertion or while the patient is at rest. Occasionally, there is no pain; in such patients the dissection proceeds very slowly.

With rupture of the intima of the aorta, the dissection begins. Symptoms and physical signs appear and vary with the extent of the dissection and the branches of the aorta involved. If dissection occurs, as it usually does, in the first four centimeters of the aorta, and if the area involved is small, the patient may have only pain and shock. Very rarely, however, does the process stop at this point, but separation of the intima and media progresses and it may involve all branches of the aorta from subclavian down to and including femoral arteries.

In the event the carotid artery is involved,

¹Professor of Clinical Medicine, Emory University School of Medicine.

²Associate in Medicine, Emory University School of Medicine.

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JAMES E. PAULLIN

the patient may have symptoms referable to involvement of the central nervous system, and they are frequently diagnosed as having a cerebral vascular accident manifested by either a hemiplegia, temporary loss of vision, unconsciousness, or other signs pointing to involvement of the central nervous system. These symptoms and signs are produced by the dissection involving the carotid arteries causing a diminution of the caliber of the vessels and interfering with an adequate supply of blood to the brain.

SYMPTOMS

MANY of these patients complain of a burning sensation over the entire body, particularly severe in the chest, the arms, and legs. Numbness and marked weakness of the lower extremities occurs frequently. Severe abdominal pain is common, and occasionally patients with this disease have been diagnosed as having either a perforative peptic ulcer or acute

appendicitis. Marked lumbar pain occurs in those patients who have dissection involving the renal arteries. Varying degrees of shock are encountered, from that in which the patient is in a stage of complete collapse with imperceptible pulse, cold, clammy skin, shallow respirations, unobtainable blood pressure, to the milder degrees of shock without marked disturbance of either the blood pressure or pulse. The degree of shock depends to some extent on the location, the extent of, and the rapidity with which the dissection occurs.

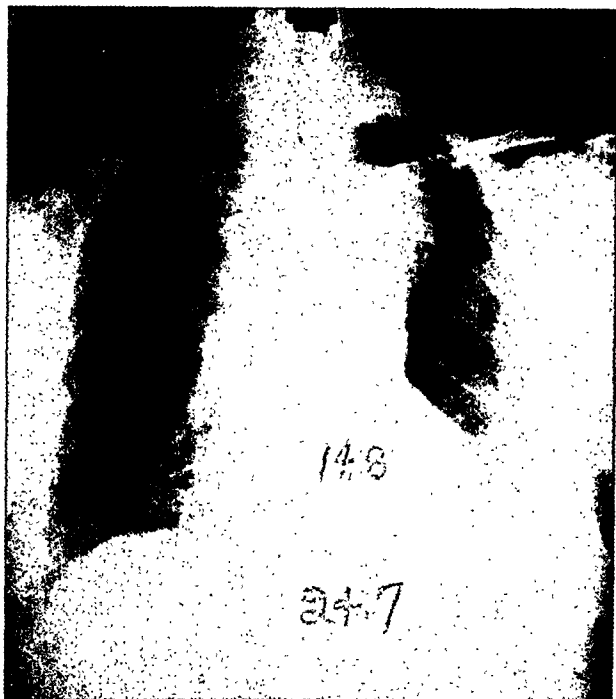
PATHOLOGY

The pathologic changes observed are interesting because at one time it was thought that syphilis played a considerable role in its causation. Now we are convinced that syphilis is not an etiologic factor. Arteriosclerosis and hypertension are the factors which are associated with and probably responsible for all cases of dissecting aneurysm of the aorta. Microscopic examination of the aorta reveals a cystic degeneration of the media, together with fragmentation of the elastic fibrils and the presence of a colloid-like material. These changes cause a weakening of the aortic wall. When hemorrhage from the vasa vasorum occurs in the media of such a diseased area, a bleb forms, stretching the intima, ultimately producing a rent which furnishes an entrance for blood from the aorta and dissection begins. In our experience, this is the most common pathologic lesion. The extent of the dissection will depend on the condition of the artery, the amount of atheroma, and height of the blood pressure.

PHYSICAL SIGNS

These vary considerably, depending on the extent and rapidity of aortic involvement. The heart is usually increased in size, particularly the dullness beneath the sternum is increased in width. There may or may not be a loud systolic or a diastolic murmur at the aortic area. A history of hypertension over a period of years may be obtained. With dissection, in

Figure 1. Chest x-ray of Case 1, demonstrating the finding of widening at the cardiac base and tortuosity of the aorta—interpreted as "consistent with a diagnosis of dissecting aneurysm."



the majority of patients, there is an inequality of the pulse; the radial pulse on one side may be easily felt, whereas it may be feeble or absent on the other. The same can be said of the carotid and femoral pulses. As dissection proceeds down the aorta, there occasionally appears in the inguinal region a nonpulsating tumor which varies in size from a mass 1 or 2 cm. in diameter to a lump 10 or 12 cm. in diameter. Such a swelling has been mistaken for an abscess and surgically drained with disastrous results. There may be a decided difference in the temperature of the extremities. The skin is usually cold or clammy with a normal or rapid pulse. The blood pressure is usually ele-

vated. Manifestations referred to the nervous system have been mentioned.

Laboratory findings do not help very much in making a diagnosis. There is a slight leukocytosis, an albuminuria, and if the renal arteries are severely involved there develops a diminished urinary excretion, increased nonprotein nitrogen of the blood, uremia, and death.

The x-ray, however, is of a great deal of value, in diagnosis particularly—fluoroscopic examination as well as studying films. Both show an increase in the mediastinal shadow with occasional displacement of the heart downward and to the left, as shown in Figures 1 and 2. With arteriography separate channels



Figure 2. Chest x-ray in Case 2, demonstrating the same widening, but at a different level.

in the aorta can be demonstrated.

The electrocardiogram usually shows a left axis deviation and at times the findings of coronary insufficiency or those of a severe coronary occlusion, as shown in Figures 3 and 4. This usually occurs only in those patients where the coronary arteries become involved in the dissection.

PROGNOSIS

THE final outcome in most of these patients is usually one of the following:

1. The dissecting aneurysm may rupture into the aorta; the original rupture which occurred just above the aortic valves may dissect for some distance along the aorta and again rupture at a distal point into the aorta. A patient with only this may live for several years. We have had one patient who lived five years after his original rupture.

2. Rupture of the aneurysm into the mediastinum where the bleeding may be confined to this area for several days or, rarely, weeks.

3. Rupture into either the pleural or abdominal cavities.

4. Rupture into the pericardium.

Your attention is directed to a consideration of the two undiagnosed cases: To describe a method of radiologic diagnosis utilized by Dr. Hans Weens of the Department of Radiology, in one of our patients; to discuss the mechanism by which pain in the extremities is produced and the therapeutic implications of this mechanism; and to discuss a method of therapy employed in one of our patients.

CASE REPORTS

In patients No. 7 and No. 8, a diagnosis of dissecting aneurysm was not made. Patient No. 7 was a 40-year-old colored maid who came to the hospital because of the sudden onset, six hours before admission, of a severe mid-back pain radiating anteriorly and accompanied by considerable dyspnea. She was known to have had syphilis for six years, which had been poorly treated. She was severely hy-

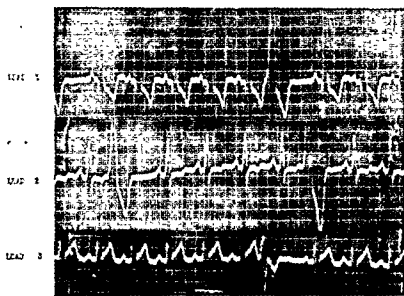


Figure 3. Electrocardiogram of Patient No. 1, showing the usual findings in dissecting aneurysm—evidence of left ventricular strain predominates.

pertensive and arteriosclerotic for several years. She had had congestive failure off and on in varying degrees for five years, as well as a tracheal tug.

An x-ray of her chest six years before the present admission showed a right mediastinal shift, rightsided atelectasis, an enlargement of the aorta, and she was diagnosed then as having syphilitic aortitis with an aortic aneurysm.

On this admission she was orthopneic and in extreme distress. The ocular fundi were quite arteriosclerotic. There was a rightsided tracheal shift, a tug was present, the heart was markedly enlarged, the rhythm was regular, and there was a systolic as well as a diastolic murmur heard over the base. Over the eighth, ninth, and tenth thoracic vertebrae there was exquisite tenderness. The liver was enlarged. All peripheral pulses were present, forceful, and of water-hammer quality. Pistol shot sounds were heard over the femorals. The Kahn blood test was positive. An x-ray of the chest revealed diffuse cardiac enlargement, extensive atelectasis of the right lung with mediastinal shift to the right and a small amount of pleural fluid. An electrocardiogram showed left axis deviation, an auriculoventricular dissociation, which was thought to be a digitalis intoxication.

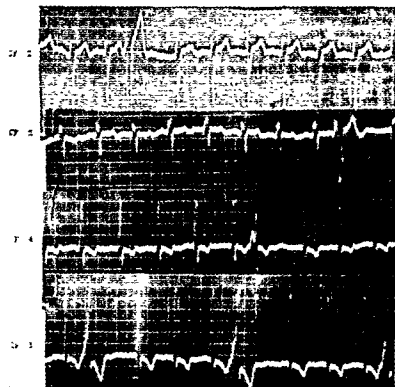


Figure 4. Continuation of electrocardiogram of Patient No. 1.

THE patient was sedated and 100 cc. of clear fluid was withdrawn from the right pleural cavity. Dyspnea constantly increased, edema of the lungs developed, and she died forty hours after admission. The chest pain persisted throughout her hospital stay.

The clinical diagnosis was syphilitic aortitis with vascular aneurysm, possibly rupture, with secondary rightsided lung atelectasis.

At autopsy, aside from generalized arteriosclerosis and general cardiac hypertrophy, an extensive dissecting aneurysm beginning at the exit of the left common carotid artery, and extending to the aortic bifurcation, was found. The only arterial branch affected was the superior mesenteric artery, along which dissection extended for 3 cm. There were small tears into the aortic lumen near the renal arterial branches, but no rupture was found superiorly. Pulmonary edema was marked.

The history of poorly treated syphilis, despite the fact that we knew syphilis was not an etiologic factor in causing dissecting aneurysm, the positive Kahn blood test, suggestive evidence of saccular aneurysm of the aorta of several years' standing, the presence of an aortic

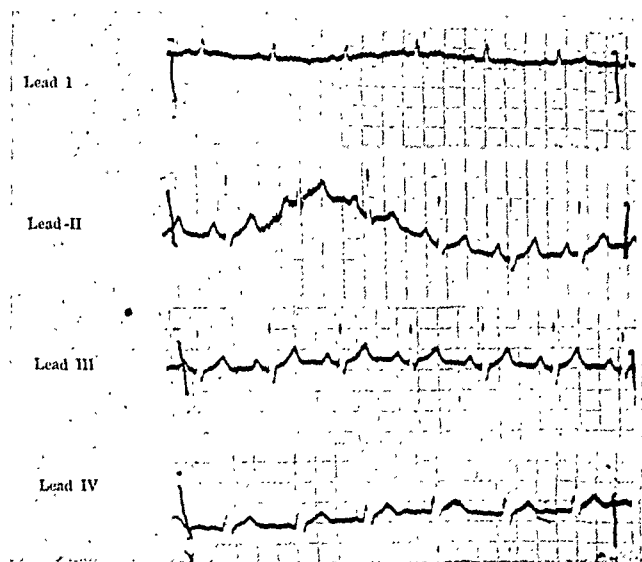


Figure 5. Normal electrocardiogram of Patient No. 9. (Dissecting aneurysm of arch and descending portion of aorta.) This was made about three weeks after the dissecting had occurred.

diastolic murmur, led us to the erroneous conclusion that we were dealing with a syphilitic aneurysm which had ruptured.

Case 8—I doubt seriously if anyone would have suspected a dissecting aneurysm in this patient. She was a 35-year-old female, the youngest patient we have seen, who was known to have had hypertension for at least a year. She was completely symptomless until less than one hour before death when, on her way to town with her husband, she complained of sickness to her stomach and at once began to vomit food she had recently taken for supper. She became comatose quickly and was admitted to the hospital.

The clinical diagnosis was rupture of the stomach, cause undetermined. She died within an hour after she reached the hospital.

The essential autopsy findings were marked subcutaneous emphysema of the anterior chest wall extending into the axillary spaces, into the neck and face, causing puffiness of the cheeks and eyes. The abdomen was markedly distended and tympanitic, and upon separating the rectus sheath the peritoneum bulged into the incision. Upon puncture of the peritoneum

much gas escaped from the abdomen. The peritoneal cavity contained 250 cc. of a cloudy fluid. On the anterior surface of the stomach there were two rents in the serosa 4 cm. and 6 cm. long. At the upper end of the short rent there was a 1 cm. tear through all layers of the stomach allowing gastric contents to empty into the abdominal cavity. There was free air in the pleural cavities and a marked mediastinal emphysema. The aorta was sclerotic and inelastic with a transverse rent 1.7 cm. long just above an arteriosclerotic plaque in the proximal portion of the ascending arch which dissected into the ascending aorta as far as a calcified plaque in the left subclavian artery, where there was another transverse rent in the intima. No connection between the dissecting aneurysm of the aorta and the rupture of the stomach could be made. The stomach contained approximately 200 cc. of semisolid material, and there were four longitudinal ruptures from which gastric contents escaped. Why these occurred, we are unable to say.

The anatomic diagnosis was dissecting aneurysm of the aortic arch, medial cystic necrosis of the aorta, hemopericardium, which caused death, hemorrhage into the stomach wall with rupture of the stomach, tension pneumothorax and peritoneum, mediastinal emphysema, generalized arterial and arteriolar sclerosis.

THE next patient we report is a 55-year-old white salesman who was well until three weeks before admission to the hospital, when, on alighting from an automobile, he had a sudden "tearing" pain located in the substernal and epigastric regions which lasted for about forty-five minutes and was relieved by morphine. The pain did not radiate; it was accompanied by moderate dyspnea and marked sweating, and left him feeling weak. At that time, a roentgenogram of his chest made in a distant town revealed a peculiar shadow in the left upper chest. Since the onset of pain he had a dry hacking cough which had diminished some by the time of his present admission. No recurrence of the severe pain had occurred, but



Figure 6. Chest x-ray of Patient No. 9, showing the normal-sized heart and the dilated descending portion of the aortic arch.

he continued to complain of weakness, loss of weight (30 pounds), and soreness which was localized under his manubrium.

Physical examination was essentially negative. His blood pressure was variable, with slight differences in the two arms, varying between 130/70, left; 150/90 mm. Hg., right. The next day, it was 156/100, left; 164/110, right. The pressure in his legs was practically the same—168/120 mm. Hg. He was quite emaciated and weak. There was a tracheal tug. The heart was normal in size, with no mur-

murs. The peripheral vessels were normal, and there was no edema. The laboratory examinations of the blood and urine were essentially negative.

An electrocardiogram made three weeks after dissection occurred was within normal limits (Figure 5).

A roentgenogram of the chest showed both lung fields to be quite clear (Figure 6). The descending portion of the aortic arch was slightly dilated.

Figure 7, an angiocardigram made by Dr.

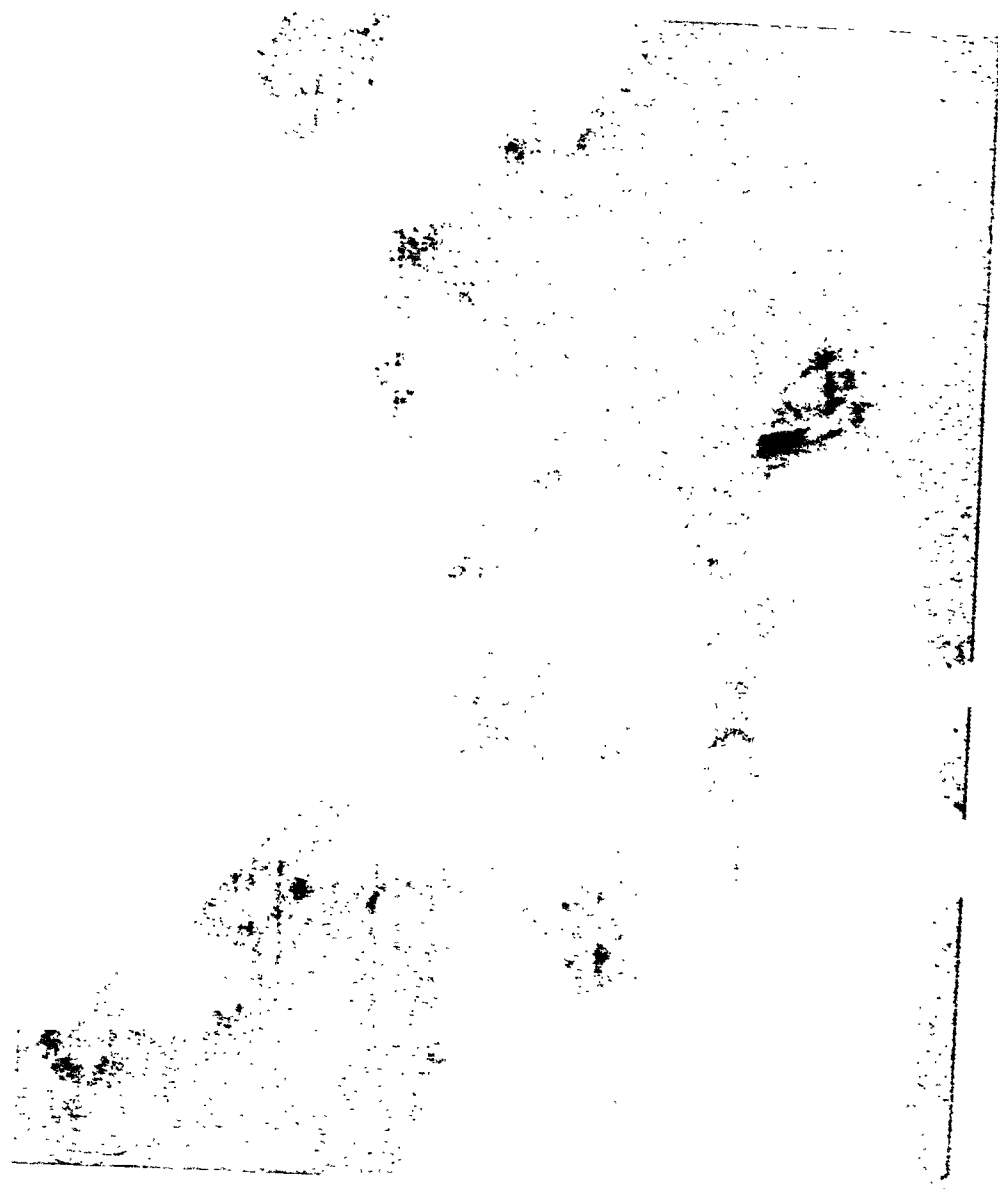


Figure 7. Angiocardiogram of Patient No. 9. This demonstrates the narrowing of the blood stream in comparison with the total opacity of the arch and descending aorta, clearly differentiating the lumen of the aorta from the area of dissection.

Weens, demonstrates the narrowing of the blood stream in comparison with the total opacity of the arch and descending aorta, clearly differentiating the lumen of the aorta from the area of dissection. The x-ray was made after the intravenous injection of 70 per cent diodrast.

This patient was operated on by Dr. Osler Abbott. (To be reported later in more detail by Dr. Abbott.) A left thoracotomy was performed. The ascending aorta was found to be rather widely dilated and the aortic arch

widened. After dissecting about 80 per cent of the aorta involved free, the vessel was wrapped as completely as possible with cellophane and cellophane projections were inserted into regions which could not be dissected free. The cellophane was sutured in place with heavy silk. The patient withstood the operative procedure well, and aside from a moderate left serosanguinous pleural effusion which was drained, he experienced an uneventful post-operative recovery and was discharged from the hospital twenty-one days later. Aside from

difficulty in gaining weight and chest soreness referred to the left shoulder, which disappeared when he was lying down, he was symptomless.

A chest x-ray two months after his discharge showed that the postoperative atelectasis had cleared, the thickened pleura at the left costophrenic angle had practically cleared, and there was a slight decrease in the size of the heart and of the aortic shadow.

Many attempts at roentgenologic diagnosis have been made, but now it is most important to localize the point of rupture if possible in order that the newer therapeutic procedure of wrapping the aorta with cellophane can be utilized and properly evaluated. Certainly now it is most important to know the localization and the extent of the rupture more than heretofore. If, on serial roentgenography, a rapidly progressive increase in the width of the aortic shadow occurs, one may feel safe in making this diagnosis. Usually, however, when the patient is first seen rupture and dissection have taken place to such a marked degree that little information can be added by serial x-ray studies.

The reasonableness of an operative approach in treating this condition is obvious but its efficiency will be evaluated by a careful study of those patients who are suitable for this type of treatment, and what the final results are on a larger series of cases than are now available.

SO FAR, most of our time has been consumed in refreshing your mind on the classical features of the disease; there are other problems connected with the etiology and pathologic physiology of the disease which are most

intriguing. Time does not permit a discussion of many of these, but one might inquire as to the cases of cystic degenerative changes in the aorta; many authors, notably Schnitker and Bayer,³ Kountz and Hempelman,⁴ and others, provide information which should be of fundamental importance in seeking etiologic factors in certain cases. What is the relationship between the metabolic changes occurring in pregnancy (where rupture occurs without the strain of labor), and rupture occurring in patients who have undergone thyroidectomy for severe hypertension?

Leg weakness with pain in the extremities should be further studied. It is generally believed that ischemia of the spinal cord due to dissection about the intercostal or other arteries supplying the cord is the cause. The condition is quite distressing and is difficult always to explain, particularly when there is adequate or good pulsation in the arteries of legs and feet.

The widespread attention given in the past to dissecting aneurysm of the aorta has resulted in more acute diagnostic accuracy and acumen. It is to be hoped that further investigation and observation of patients will be of great value in preventing its occurrence.

REFERENCES

1. McGEACHY, T. E., and PAULLIN, J. E.: Dissecting aneurysm of the aorta. *J.A.M.A.* 108:1690-1698 (May 15) 1937.
2. LOCUT, R. BRUCE: Dissecting aneurysm of the aorta. *Am. J. M. Sc.* 206:54-66 (July) 1943.
3. SCHNITKER, MAURICE A., and BAYER, CHARLES A.: Dissecting aneurysm of the aorta in young individuals, particularly in association with pregnancy, with report of a case. *Ann. Int. Med.* 20:486-511 (March) 1944.
4. KOUNTZ, WILLIAM B., and HEMPELMAN, LOUIS H.: Chromotropic degeneration and rupture of the aorta following thyroidectomy in cases of hypertension. *Am. Heart J.* 20:599-610 (November) 1940.

Benadryl*

FOR RELIEF OF ALLERGIC SYMPTOMS: BY INJECTION

SAMUEL J. TAUB

CHICAGO

THE recognition that histamine is released by sensitized cells into the blood stream and is responsible for many of the symptoms occurring in urticaria, serum sickness, drug allergy, hay fever, asthma, and allied illnesses has now been fully demonstrated.¹ The local application of a solution of any of the antihistaminic drugs to a scratch on the skin inhibits the normal whealing from histamine or that from an antigen such as grass or ragweed pollen in an allergic individual.

The mechanism of this inhibition has not been fully understood, but it is believed that benadryl and pyribenzamine act by displacing histamine in the tissues.² It has been shown that the oral use of benadryl in 50 to 100 mgm. doses did not have any decisive effect on the whealing produced on scratch tests with serial dilutions of histamine or with ragweed extract in sensitive patients. When a solution of benadryl was mixed with the histamine or ragweed extract, or when it was applied to scratches prior to the application of these wheal-producing agents, there was a marked inhibition of the wheal phenomenon.³

In February 1945, Loew, Kaiser, and Moore published their results with benadryl in preventing fatal experimental asthma in guinea pigs exposed to atomized histamine.⁴ And in March 1945, these authors were able to prevent anaphylactic shock in guinea pigs with synthetic benzhydryl alkamine ethers (benadryl).⁵ Numerous articles have appeared in the literature since March 1945 by many clinicians on the use and results obtained with benadryl

and pyribenzamine. Numerous observers have reported many side effects from each of these drugs, chiefly drowsiness, sleepiness, nervousness, fatigue, ataxia, epigastric distress, bad taste, tingling of the extremities, hysterical reaction, stupor, narcolepsy, confusion, palpitation, somnambulism, muscular aching, and acute melancholia.⁶

McElin and Horton described a prolonged reaction to benadryl, occurring on a dosage of one to three 50 mgm. capsules of benadryl a day; after one week the following effects were noted: puffiness of the eyes, three stools a day, considerable flatus, feeling of tightness in the arms from the shoulders downward, numbness of the hands, and a difficulty in coordination of thoughts and speech.⁷

The gastrointestinal symptoms are explained as due to decreased histamine and diminished secretion of the stomach. Mental lethargy, drowsiness, and weakness are intensifications of side reactions. Numbness and tingling of the extremities are normal side reactions. There are enough unpleasant side reactions from these drugs to make them a handicap in their use and to limit the size of the doses.

For these and other reasons, a solution of benadryl containing 10 mgm. of the drug per cubic centimeter was tried intramuscularly in patients who did not react well on the usual doses of benadryl and pyribenzamine by the oral route. One patient had a severe urticaria and angioneurotic edema of three months' duration; her private physician had prescribed large amounts of benadryl and pyribenzamine by mouth but she received no benefit from them. It was impossible to test her because of

*Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride.

the irritable and diffusely whealing skin. One cubic centimeter of benadryl (10 mgm.) injected into the deltoid muscle resulted in a complete disappearance of all whealing and swelling within ten minutes. There were no side reactions, and the effect was dramatic. This single injection resulted in a complete disappearance of all urticarial lesions for the first time in three months, and the relief persisted until she returned the next day (twenty-four hours later), when a few urticarial lesions were present along both arms. It was possible to do complete intradermal tests on this patient ten to fifteen minutes after the intramuscular injection of 1 cc. of benadryl solution. Crabmeat gave a very severe local reaction, which also was accompanied by a new appearance of generalized urticaria and angioneurotic edema within five minutes following the intradermal test. A complete disappearance of these lesions occurred following the use of 1 cc. of benadryl solution intramuscularly.

BENADRYL solution quickly relieves itching in atopic or allergic dermatitis, serum and drug allergy, angioneurotic edema, urticaria, and contact eczema. Its use in several patients with an acute asthmatic paroxysm was of no benefit. In pollen hay fever and perennial allergic rhinitis no distinct advantage was noticeable in comparison with the use of this drug by mouth. Dramatic relief was noted in 3 patients with marked nasal blockage due to the rebound action from the prolonged use of nasal vasoconstrictors.

It can be concluded that benadryl solution for intramuscular or intravenous use in 1 cc. doses (10 mgm. of benadryl) is a valuable addition to our therapeutic armamentarium. The



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undesirable side reactions mentioned previously are avoided, and it is possible to control severe allergic symptoms quickly with a minimum amount of the drug. One of the most valuable uses is the control of dermatographia and urticaria during the period that intradermal skin testing is attempted for diagnosis.

It must be emphasized that this type of therapy including other antihistaminic drugs does not replace skin testing to determine the etiologic factors, nor is it a substitute for thorough allergic management needed to control various allergic manifestations seen in practice.

Benadryl solution used was supplied through the courtesy of Parke Davis & Co.

REFERENCES

1. TAYLOR, SAMUEL J.: *Essentials of Clinical Allergy*. Baltimore, Williams & Wilkins Co., 1945.
2. WELLS, T. A., and MORRIS, A. C.: Observations on the antagonism of histamine by benadryl. *Federation Bull.* 4:149, 1945.
3. FRIEDLANDER, S., and FLEISCHER, S. M.: Histamine antagonists. *J. Allergy* 17:129 (May) 1946.
4. LOEW, E. R., KAISER, M. E., and MOORE, V.: Synthetic benzhydrol alkamine ethers effective in preventing fatal experimental asthma in guinea pigs exposed to atomized histamine. *J. Pharmacol. & Exper. Therap.* 83:120-129, 1945.
5. LOEW, E. R., and KAISER, M. E.: Alleviation of anaphylactic shock in guinea pigs with synthetic benzhydrol alkamine ethers (*β*-*dimethylaminoethyl benzhydrol ether* and *β*-*morpholinomethyl benzhydrol ether*). *Proc. Soc. Exper. Biol. & Med.* 58:235-237 (March) 1945.
6. WATSON, G. L.: Clinical results with benadryl. *J. Allergy* 17:142-144 (May) 1946.
7. McELIN, T. W., and HAYES, B. T.: Clinical observations on use of benadryl: new antihistamine substance. *Proc. Staff Meet., Mayo Clin.* 29:417-429 (November) 1945.

DIAGNOSTIC CLINIC

The Unknown Diabetic

ELLIOTT P. JOSLIN*

BOSTON

THE UNKNOWN diabetic is an important factor in the revolution of the practice of medicine. The unknown diabetic is changing the doctor's status and more and more placing him in the employer class. I shall try to illustrate these two ideas in this presentation.

How many unknown diabetics are there in this country? The Oxford survey gives the answer. I know the town of Oxford well; it is just south of Worcester, Massachusetts. It is accustomed to diabetics because for sixteen years we have had over 100 diabetic children at camp each year in the town. The doctors in the town are familiar with the camp. The United States Public Health Service made a survey there last year, and learned from the doctors that there were 40 known diabetics in the town. However, when blood and urine examinations were done on 3,500 of the 5,000 inhabitants, they discovered that there were 30 unknown diabetics. (This was the first time such a survey had been done on a large scale in the history of the world.) If all of the people had been tested, it is quite obvious that there

would have been one unknown diabetic to match each one known.

For some years I have considered the number of diabetics in this country to be a million. Proof of this came from a survey conducted with the help of the Medical Society of Arizona a few years ago in which we were able together to demonstrate that diabetes was just as common in Arizona as in the states where the death rate for diabetics was said to be four times as great: 10 in Arizona, 40 in some of the eastern states. We found that diabetes was just as common among Indians, inmates of prisons, and in the insane asylum, and just as common in the people generally and even among the doctors themselves as it was in such states as Rhode Island and New York.

Statistical studies led to the conclusion that the number of diabetics in this country was easily a million. These facts were buttressed by the reports of Blotner in Boston, Gates at Niagara, and by Olaf Hanssen in Bergen, Norway. We have a million known diabetics in the country and the Oxford survey brings out the fact that there is another million unknown.

How are you then to discover the unknown diabetic?

Age—Only one-third of the diabetics are under 40 years of age. There is no use looking

*Clinical Professor of Medicine, Emeritus, Harvard Medical School.

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THE UNKNOWN DIABETIC: JOSLIN

through schools to pick out the diabetics; 2,500 boys must be examined to find one diabetic, or 2,500 girls, whereas after 65 years of age only 70 men or 45 women must be examined to disclose a case.

Sex—Females are more common than males in the diabetic group, but this is true only of females who have borne children. The incidence of diabetes in females who have not borne children resembles more that of the men.

Obesity—Eighty per cent are more or less overweight. If a woman comes into your office who is over 40 years of age, has borne children, and is obese, diabetes may be staring you in the face.

Heredity—A family history of diabetes is a very easy way to find the new diabetic. If you have one diabetic twin and it is an homologous twin, you know the other twin will come down with diabetes or already has it. You know that among all the patients the heredity is very high, even though they may not know it. The patient may say there is no heredity; but I learn that a sister has the disease. In fact, she has been my patient but has kept knowledge of it concealed. Recently in one history I found a patient who was an adopted child and never knew about her parents. Factors such as this make statistics faulty. I showed a man last week to a group of doctors; he was found to have diabetes at the age of 18 years, and there was no family history of the disease. About twelve years later, however, his brother was found to have it, and subsequently his mother learned that she also had diabetes. If you have one case in a family, I ask—who gave you diabetes? It is that patient's duty and interest to find out. In this way other unknown cases become known.

If you see a patient with diabetes, remember the incidence of obesity. Never allow a relative of a diabetic to leave your office without weighing him or her and calling to his or her attention the danger of the relatives of diabetics acquiring the disease because they are fat.

Jews—Diabetes is twice as common in Jewish as in non-Jewish people.



ELLIOTT P. JOSLIN

Chemical examination of the urine is important, but it is more important to examine the urine and blood sugar after a meal. Only a few cases are picked up by the fasting blood sugar or fasting urine. You are looking for new cases; you want to test the urine and blood sugar after a meal. It may be that there are some with a blood sugar of 170 who do not have diabetes, even though they have an accompanying glycosuria, but the number is few and they can be studied and eliminated later. Our diagnostic criteria demand glycosuria and a blood sugar fasting of 130 or 170 mg. after a meal.

Fortunately there is now a new blood sugar test which can be done in five minutes; this method will probably be published soon. We are beginning to use this method. In the course of the next year I am positive that there will be given to all of us blood sugar tests which will allow us to screen our patients very simply, easily, and much better than ever before.

Of what does this new clientele of 1,000,000 diabetics consist? The bulk of all diabetics is in

the lower income group, just as in other diseases; especially the unknown diabetics are in this group. I can illustrate this best by citing the patient whose diabetes is first discovered after he has entered the hospital in diabetic coma.

In Indianapolis last fall Dr. Peck collected for me 10 patients who had recovered from diabetic coma. When I studied them carefully, I found that none of those patients knew that he or she had diabetes until recovery from coma. I think it is truly wonderful that they could have 10 recoveries ranging from the first decade to the eighth and ninth decades of life. In our own group, 19 per cent of our cases never knew they had diabetes until they had recovered from coma in the hospital. Thirty-five per cent of Dr. Dillon's group in Philadelphia were not aware they had diabetes until they had recovered from coma. Here is an example in this patient from the St. Louis City Hospital who recovered from coma without ever knowing that she had diabetes; that was in 1939. This is a special group among the unknown cases—the emergency group, small but urgent. They exist everywhere. In Indianapolis there was a great rush of people from below the river for work during the war and this is one reason they had not been evaluated or picked out.

Thanks to Dr. Sexton, I bring in this patient to drive home the point of the unknown diabetic, and incidentally that unknown diabetics are often in the lower income group.

A characteristic of the "unknowns" is that they are early, mild cases and therefore they are overwhelmingly cases amenable to treatment. Years ago Naunyn brought out the fact that the severe case of diabetes treated vigorously often did remarkably well and the mild case neglected did badly. All the work that has been done on diabetes has confirmed this.

Years ago we took the diabetic doctors among our group of patients and proved that they did much better than others. We saw the same phenomenon among cases discovered by insurance examiners; the reason was that the disease was caught earlier and so was amenable to treatment. This fact, that the unknown mil-

lion diabetics in the country, often symptomless, are the ones that are the most hopeful, who do the best and live the longest, cannot be emphasized too much. The insurance companies surely should take notice of them. In the last year fourteen of the insurance companies have been insuring some of our patients, (subsequently I learned forty-six companies are insuring diabetics;) but they are just reaching the stage where they can double the number of diabetics they insure, and double them among the group that will live the longest and do the best, because they are the ones, with the exception of this group of coma cases, who are caught in an early phase of the disease.

HOW ARE doctors going to treat an extra million diabetics? Today you are swamped with work. That is why I think the million diabetics will help to revolutionize the practice of medicine and will change the doctors from their present status more and more into an employer group.

We know that the aim of treatment is to control the disease. We know that we can abolish all the symptoms and signs of the disease. But how are we to control it? Recently the beautiful work done in Philadelphia by Dohan and Lukens was published. They have shown a new way of causing diabetes. They have taken a healthy cat and then produced artificially hyperglycemia; at the end of two weeks that cat was a diabetic. We have different methods of producing diabetes: giving alloxan; taking out the pancreas; injecting anterior pituitary extract. But the method of Dohan and Lukens goes further, because it carries with it for you and me a therapeutic handle. They showed that hyperglycemia in their cat will result in injury to the islands of Langerhans within two weeks and the cat would come down with diabetes.

If hyperglycemia will cause diabetes in a healthy cat with an undamaged pancreas, think how we must work against hyperglycemia in our diabetics who already have a damaged pancreas.

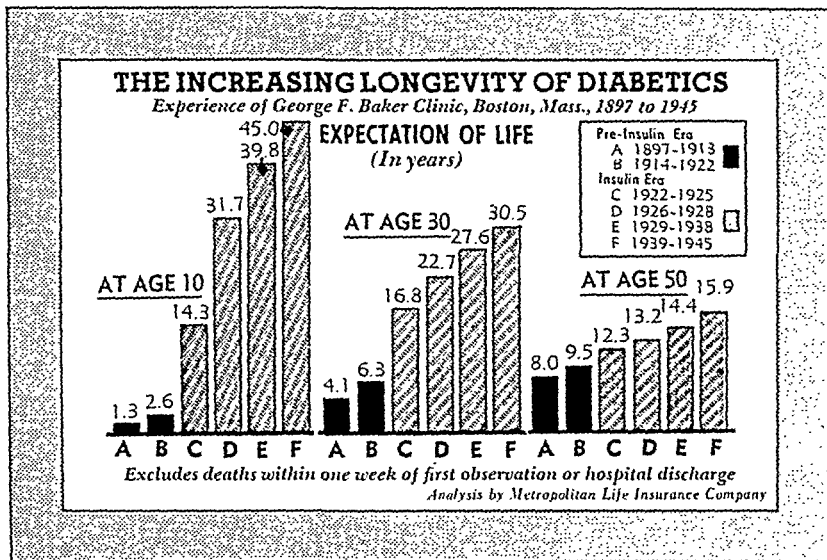


Figure 1.

A further point in their work which is important for us is that they were able to demonstrate that if, after the diabetes had been produced, they brought the blood sugar down to normal by diet, by insulin, or even by phlorhizin, within a reasonable time they could reverse the process and cure diabetes in the cat. As yet, this cannot be done in a human being, but their work is very encouraging and significant for each one of us. That is the aim we have before us.

How are you going to treat these additional million diabetics? By education of the patient. You cannot do it yourselves; you must have somebody to help you; you must have secretaries or nurses or nutritionists or dietitians. We cannot get them today or the range in salary is so high that we cannot afford such luxuries. What we must do, therefore, is have nurses' aides, educationists, high school girls, somebody who has the zeal and the desire to

be helpful, and to train them to put across this education to the patients.

Only a few patients can go to the hospital. Our patients who are hospitalized now have had the disease an average of ten years. When I began talking before this Association my average case was dead in five years; now they live an average of over fourteen years.

Everyone should try to get a nurses' home available or get a diabetic to take in another patient. Nurses' homes can take a patient in on a Monday and send him home well-trained the following Saturday.

This all means that one must bring up a new class of people, more nurses' aides, more young people who have not been obliged to go through long years of training, who will help to teach the elemental things under your supervision to your patients. In other words, one must expand one's office force. The nurse in the office and the aides under her can nurse the

patient along from day to day, under the doctor's supervision, just as well as the doctor does in the hospital, and that is what must be done.

I am very fond of horses. I have a farm. While coming out here on the train I looked for horses working on farms. I did not see a single horse. We are building a boys' camp now, a lovely camp—somebody gave us the money for it. How are we doing it? We got a bulldozer to make the road and the ball park and the swimming beach. That bulldozer does more work in a day than a pair of horses and two hard-working men used to do on my farm, years ago, in one or two weeks, and the bulldozer wasn't tired at the end of the day; neither was the man who drove it.

We can't all have a bulldozer in the office, but we must have the equivalent if we are to treat these diabetics, because there are a million of them and they are in the lower income group and need our attention.

What are the results of treatment? I want especially to show you that there is more ahead in the treatment of diabetes than even in the past. It is reckoned by the Metropolitan Life Insurance Company that the death rate for our cases at the age of 10 years has dropped 99 per cent. Our death rate has fallen all along the line, but Figure 1 will bring out the fact that the treatment of diabetes has improved and is giving results.

Figure 1 shows my figures on some 8,300 dead diabetics plus several times as many living diabetics in three age groups: 10 years, 30 years, and 50 years. The point I wish to make for each one of you is that if you look at any of these groups you will see that there is not a break in the series. As you move from left to right showing successive periods of observation, beginning way back between 1898 and 1914 and coming up to the present, in each column you will see a record higher and better than the last. Not once from 1898 to 1947 has there been a break in the improvement of expectancy of life of diabetics 10, 30, or 50 years of age. That one fact I wish to leave with you because it encourages us all to go ahead. We can't conceive that progress will cease.

WE OFTEN hear pessimistic reports about diabetes. Recently it has appeared that arteriosclerosis, which we know is common, is the cause of death in 67 per cent of these cases as compared with 17 per cent prior to 1914. As a matter of fact, arteriosclerosis has replaced coma. Coma was the cause of death in 64 per cent and is now the cause in 3 per cent; arteriosclerosis is now the cause of death in 67 per cent and was the cause in 17 per cent. But the idea that I wish to drive home is that today, even after twenty-five years of insulin, a diabetic can be free from arteriosclerosis. We have proof of it. Dr. Priscilla White most assiduously has collected the statistics of 200 of our 350 diabetic children who have lived over twenty years with diabetes. I will allow that 92 per cent of them show arteriosclerotic troubles, in their eyes, in their hearts, or their kidneys, but we have 8 per cent, 16 of those 200, who do not show arteriosclerosis, who are sound today, and that should be emphasized.

We have gone steadily ahead in the treatment of diabetes. We know that we have 8 per cent free from arteriosclerosis after twenty-five years of the disease, and we expect to have 9, 10, and 11 per cent, and far, far more, who are free from it.

Years ago we used to give medals to people who lived longer with diabetes than their neighbors who did not have it. Now the Diabetic Fund at the Boston Safe Deposit and Trust Company will award a new medal to those who have had diabetes for a quarter of a century with onset under 25 years of age and show no arteriosclerosis as demonstrated by examinations of the eyes by ophthalmologists and examinations of the blood vessels by roentgenologists and by clinicians.

I always like to talk to this audience because my job in life has been to treat patients and I know that this group pre-eminently is made up of doctors who treat patients. Therefore today may I leave with you one million more patients, one million more diabetics, and I beg you to treat them vigorously, to treat them so as to control the disease, because that is your opportunity and also your duty.

Subarachnoid Hemorrhage and Intracranial Aneurysm

HENRY G. SCHWARTZ*

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

WITH THE acceptance of lumbar puncture as an almost routine technic, subarachnoid hemorrhage of non-traumatic origin has become sufficiently common to be recognized as a significant factor in vital statistics. It occurs as frequently as primary intracerebral hemorrhage or apoplexy, and obviously becomes an illness of considerable importance to the physician in general.

Although "spontaneous subarachnoid hemorrhage" appears frequently as a diagnosis, the presence of blood in the spinal fluid is a symptom or sign rather than a disease. To attempt to cope with it without understanding the causative factors would be similar to treating the fever of meningococcus meningitis by the same method we would use in fever due to peritonitis.

Blood may enter the subarachnoid space in one of several ways. Hemorrhage from the surface of the brain may rupture into the pia mater, a deep cerebral hemorrhage may break into the ventricle, or hemorrhage can occur from one of the vessels in the subarachnoid

space itself. It is the last type which is considered as primary subarachnoid hemorrhage.

The development of signs of increased intracranial pressure will depend upon the amount of bleeding and its persistence. If hemorrhage is great and if it remains unchecked, coma and death result. Symptomatically, hemorrhage usually results in sudden onset of headache, vomiting, stiff neck, dizziness, drowsiness which may develop into stupor and coma, chills and fever, and in about 17 per cent of cases, convulsions and paralysis. Most of these symptoms can and do occur with meningitis and are due to the mechanical and irritating effects of blood in the cerebrospinal fluid. Indeed, given such a picture in a previously healthy individual, the syndrome is diagnosed frequently as meningitis or encephalitis until lumbar puncture reveals bloody fluid.

Additional abnormal findings may appear, with involvement of the pupils or third nerve paralysis. Depending upon the site of the hemorrhage and involvement of adjacent cerebral tissue, one may also find other localizing signs.

Distinctive features of the spinal fluid following this type of hemorrhage are the following: (1) There is an even admixture of blood so that later specimens collected at the same puncture are as bloody or more so than the

*Professor of Neurological Surgery, Washington University School of Medicine, St. Louis.

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HENRY G. SCHWARTZ

first specimen obtained. (2) Despite gross blood there is no clot. (3) After twenty-four hours the supernatant fluid is usually xanthochromic.

The causative factors in spontaneous subarachnoid hemorrhage were for a long time considered to be numerous; and in the early literature we find among the prominent etiologic factors mentioned, arteriosclerosis, alcoholism, syphilis, pernicious anemia, aneurysm, brain tumor, and eclampsia.

In 1924 Symonds pointed out that aneurysm of the intracranial arteries was a very common cause and could be diagnosed during life. Subsequently with attention directed toward this possibility, more and more aneurysms have been looked for and found, so that it has become fairly well established that rupture of a congenital arterial aneurysm is by far the most common cause of so-called spontaneous subarachnoid hemorrhage.

As opposed to primary intracerebral hemorrhage or apoplexy where physical effort and

hypertension appear to be precipitating factors, the onset of subarachnoid hemorrhage due to rupture of an aneurysm frequently occurs during ordinary activity or even sleep.

BEFORE going on to a detailed consideration of aneurysms and the possibilities of radical therapy, it would be wise to evaluate as well as we can the prognosis in the average case. On the basis of most reports, the mortality rate following rupture of an aneurysm is about 50 per cent. Although a small percentage of cases may be diagnosed correctly before signs of leakage appear, a large bulk will not be seen until after at least the first hemorrhage occurs.

If 50 per cent of these cases recover from the initial insult, what are their chances of further trouble? The incidence of recurrence has been reported varying from 16 per cent to well over 50 per cent, and it is conceded by all that recurrences do occur and their threat is a constant source of anxiety to the patient and the doctor. Just how treacherous this condition may be was emphasized by Dandy, who described one case with recurrent hemorrhage and death eleven years after a previous episode.

In the face of poor prognosis, both as regards the immediate attack and subsequent recurrences, it seems justifiable to consider active forms of therapy in these cases. It has been not uncommon for surgeons to ligate the carotid artery in the neck in some of these patients. The effect of this extracranial ligation is assumed to be reduction of pressure and protection against subsequent rupture. The results have been variable. It has long been pointed out that in selected cases direct intracranial attack would be ideal if the hazards were not too great. No greater stimulus to this form of direct treatment could have been obtained than when Dandy published his monograph in 1944 in which he reported 36 operations with a mortality rate of 25 per cent.

If an aneurysm can be demonstrated and if its location suggests that it is amenable to surgery, the question comes up as to the time for

surgical intervention. Opinions vary. In a few instances early surgery appears to offer something to an otherwise hopelessly ill individual. On the other hand, in many cases the patient's condition is so precarious that the actual risk of any manipulation seems too great.

In the acute phase of the first few days it is desirable to keep the patient as quiet as possible and, if he is conscious, to relieve his headache and anxiety. For this purpose the barbiturates, chloral hydrate, codeine, and aspirin are most helpful.

As in other conditions with increased intracranial pressure, morphine should not be given. Elevation of the head of the bed is believed to aid cerebrospinal circulation and tends to relieve headache. Most men now agree that repeated spinal puncture is dangerous, therefore spinal puncture is advised only for diagnosis and then only a small amount of fluid should be removed.

In those cases where aneurysm is not demonstrated and where the patient improves very rapidly there is a great temptation to get him up too quickly, particularly in this day of early ambulation. If we consider that it takes at least four weeks for a clot to become organized, it is obvious that in unoperated cases a period of six to eight weeks of complete bed rest is desirable.

There are three types of aneurysms: mycotic, arteriosclerotic, and congenital. Mycotic intracranial aneurysms are uncommon and when they do occur there is a history of bacterial endocarditis. Arteriosclerosis as a cause of aneurysms of the smaller intracranial vessels is rare. It is generally agreed that most intracranial aneurysms are of congenital origin. The majority involve the anterior rather than the posterior circulation, and in turn the anterior part of the circle of Willis is predominantly the favorite site of these lesions.

IN THE drawing (Figure 1) of a view from above, the normal intracranial arterial circulation is seen. Focusing attention first on the circle of Willis it should be pointed out that

the length of the intracranial portion of the carotid is rather considerable before it bifurcates into the middle cerebral and the anterior cerebral arteries. In a reasonably young individual the intracranial carotid may be occluded, and circulation of the anterior and middle cerebrals maintained by collateral blood supply through the anterior communicating artery.

Figure 1 also demonstrates the relationship of the cranial arteries to the cranial nerves before they leave the skull. The close proximity to the optic chiasm explains how visual disturbances can occur with aneurysms of the anterior cerebral and internal carotid arteries.

The third nerve is particularly vulnerable to swelling of the internal carotid, posterior communicating, middle cerebral, and posterior cerebral arteries. The fourth and sixth nerves supplying the rest of the ocular muscles are also commonly involved. Pain and sensory disturbances about the eye and forehead are due to compression of the first division of the trigeminal by aneurysms close to the cavernous sinus portion of the carotid.

As far as the posterior cranial vessels are concerned, it is clear from this drawing that symptoms of facial palsy, tinnitus and deafness, and swallowing might occur as a result of aneurysms arising from the branches of the vertebral and basilar arteries.

The third cranial nerve is most commonly affected in cases of aneurysm of the circle of Willis. The appearance of oculomotor palsy occurring suddenly should certainly make us consider an aneurysm of the circle as the most likely diagnosis.

Hemorrhage into the frontal lobe may also occur in lesions arising from portions of the circle of Willis, particularly from the anterior communicating or anterior cerebral artery. A middle cerebral or carotid aneurysm may rupture laterally into the adjacent temporal lobe. Depending upon the site of rupture and the amount of blood which is driven into the substance of the brain, we frequently find hemiplegia, aphasia, and hemianopsia, all of which are signs of considerable localizing value. The feasibility of surgical attack will depend upon

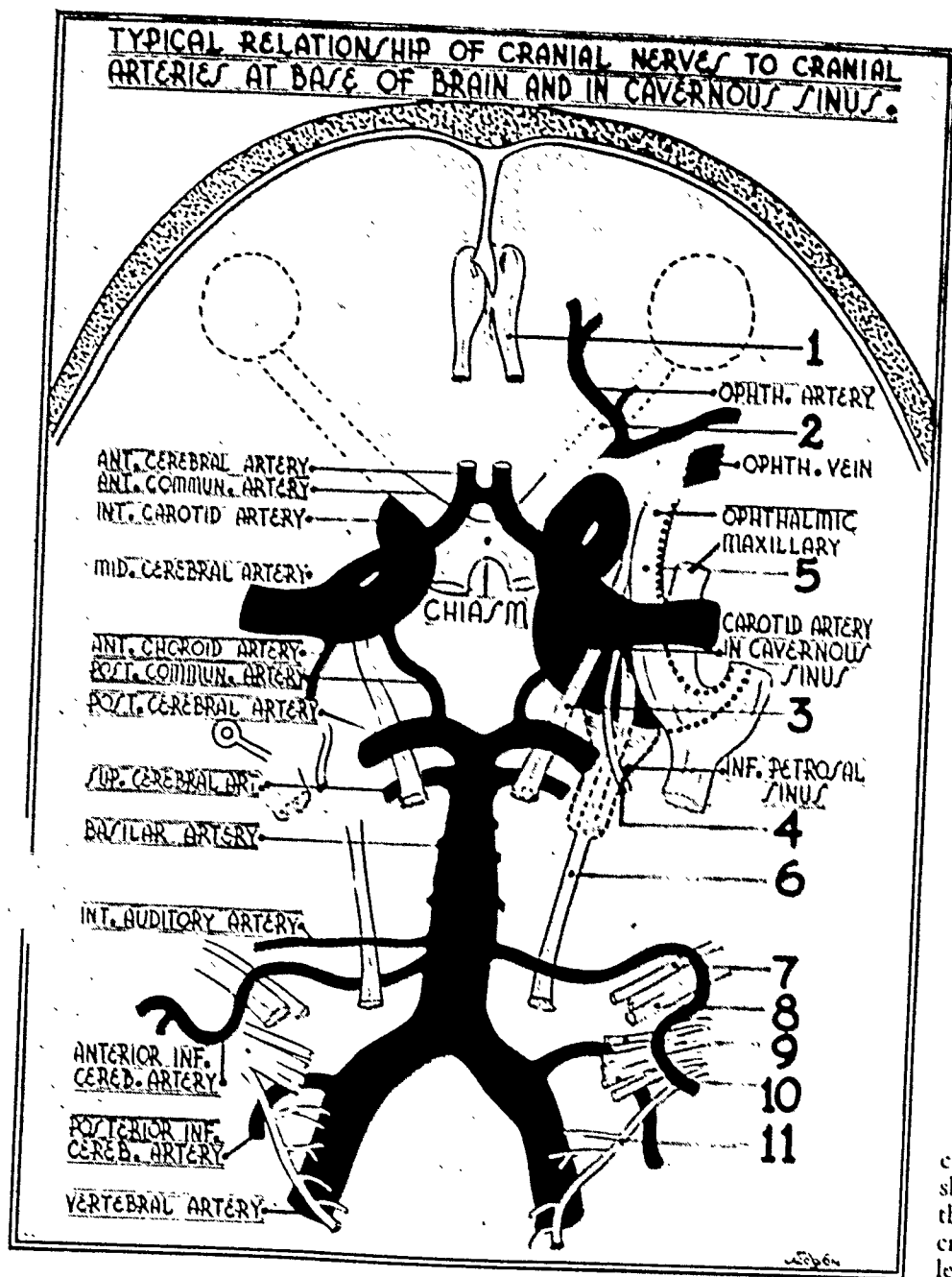


Figure 1. Normal intra-cranial arterial circulation, showing the relationship of the cranial arteries to the cranial nerves before they leave the skull.

the exact point of origin of the aneurysm.

Roentgenographic visualization was described by Moniz of Portugal. The method has been of great value particularly in outlining the anterior cranial circulation. Both thorotrast and diodrast are generally used, with most neurosurgeons preferring diodrast. The medium is injected through the carotid artery

in the neck, and x-ray films of the skull are made as the material is injected.

Figure 2 is an angiogram of a patient with unilateral third and fifth nerve paralysis and hemiparesis. It shows clearly a sacculated aneurysm. You can see the cavernous portion of the carotid artery outlined, and the sacculated aneurysm arising from the intracranial portion

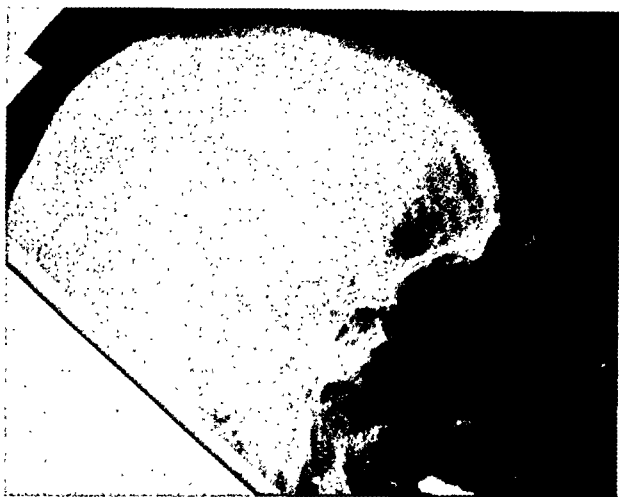


Figure 2. Angiogram of a patient with unilateral third and fifth nerve paralysis and hemiparesis, showing a sacculated aneurysm.

of the carotid before its bifurcation into the anterior cerebral and the middle cerebral. A lesion at this point is operable.

Figure 3 is an angiogram which shows a large sac arising from the middle cerebral artery. This is on the left side in a righthanded individual. Although the patient is young, direct surgical attack would not be advisable in view of the tremendous intellectual deficit that would result from cutting off the left middle cerebral blood supply.

Aneurysms of the posterior cranial circulation are less common than are those occurring anteriorly, and the congenital sacculated type is infrequently encountered. Vertebral artery angiography has thus far not been satisfactory, and in the absence of localizing signs, localization of lesions to this area is not generally possible. However, in many cases clinical localization may be quite accurate.

It is clear from Figure 1 that the close relationship of these vessels of the posterior circulation to the cranial nerves from the root of the fifth through the eleventh can give us

invaluable localizing signs and also explain how the symptomatology is frequently similar to that of eighth nerve tumor. Pathologic reports of posterior fossa aneurysms have been numerous, but successful surgical attack has not been previously reported.

I wish to present such a case today. This patient, a 27-year-old housewife, gave a history of eight or nine episodes of sudden onset of occipital and frontal headache and dizziness in a period of three years. Some of these attacks were sufficiently severe to keep her inactive for three to four months at a time.

On August 15, 1946, she had a sudden onset of occipital headache which roused her from sleep. The next morning she had staggering gait followed by nausea and vomiting. She was treated by a local physician with saline purgatives and obtained temporary relief of the latter symptoms.

Eleven days later she again had severe headache accompanied by roaring in the left ear,

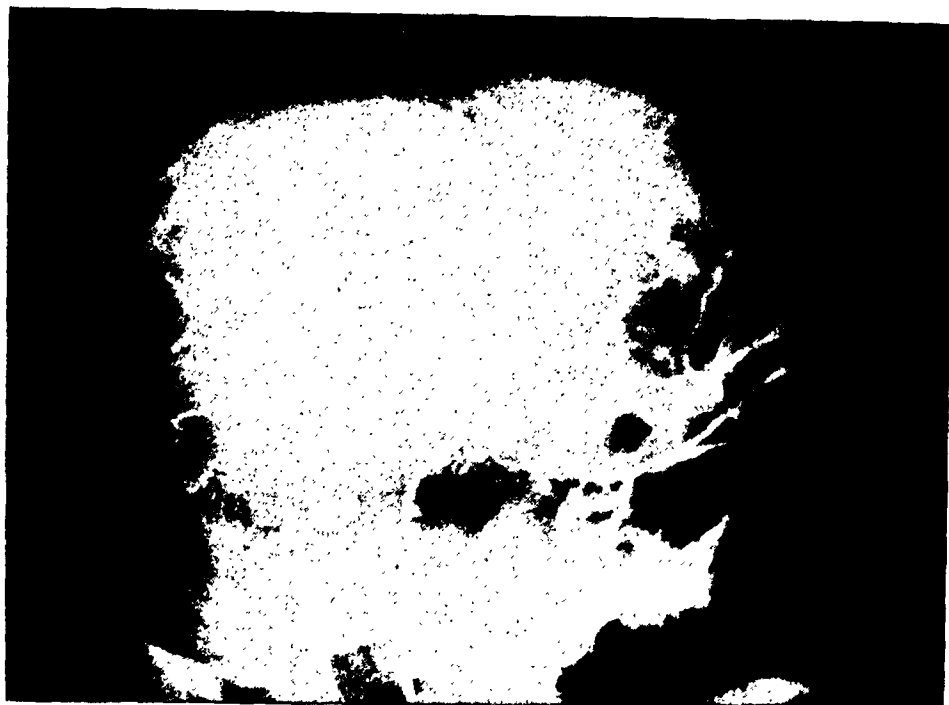


Figure 3. Angiogram showing a large sac arising from the middle cerebral artery. This is on the left side in a right-handed individual.

numbness of the left side of her face, and diminished hearing on the left. She had been seen by an otolaryngologist who found the forementioned cranial nerve signs and referred the patient to me on October 3, 1946. She was treated with bed rest, with considerable improvement in all her symptoms and was transferred to Barnes Hospital on October 13, 1946. At that time there was hypesthesia of the left side of the mouth, bilateral nystagmus, and diminished hearing in the left ear. Spinal puncture showed normal pressure. The fluid was colorless, but contained 360 red cells, most of which were crenated.

With these findings a diagnosis of ruptured aneurysm of the left cerebellar pontine angle was made. Although the patient had practically recovered from the last attack, with her long history in a young woman obliged to be active it was felt that hemorrhage would recur later and put her life in considerable jeopardy. Surgery was recommended and accepted.

A unilateral left suboccipital craniotomy was performed on November 6, 1946, and the left side of the brain stem was exposed. A small

sacculated aneurysm was found lying against the pons between the fifth and eighth nerves. It was dissected free from the brain stem and the artery was clipped on both sides and coagulated proximally. The postoperative course was uncomplicated. There was complete recovery of hearing, and neurologic examination was negative when she left the hospital on November 19, 1946, thirteen days after operation.

Since leaving the hospital eleven months ago she has remained well and happy and has had no further symptoms. We feel that this woman has been saved from inevitable death due to subsequent rupture of the aneurysm. She has no cerebellar signs or ataxia. Her gait is undisturbed. So far as the cranial defect goes, the incision was a longitudinal one, well within the hair line. There is a very small bone defect covered by muscle, and she is not in any danger of subsequent trauma.

THUS far we have discussed the most common cause of spontaneous subarachnoid hemorrhage. Certainly rupture of arterial aneu-



Figure 4. Combined air film and angiogram showing an obvious arteriovenous aneurysm in a 9½-year-old boy.

rysm accounts for the majority of cases in adults. In children, however, pure arterial aneurysm is rare, and when hemorrhage occurs in children the possibility of rupture of an angioma or arteriovenous aneurysm should be kept in mind. Pilcher of Nashville has recently reviewed the literature, which has been generally pessimistic in its attitude with regard to the possibility of eradicating such lesions, and has reported 3 cases in which angiomatous malformations of the brain were brilliantly extirpated. In his 3 cases convulsions were present, and this is a common symptom. Spontaneous subarachnoid hemorrhage occurred in one. We recently had a case in which the first signs or symptoms were due to massive hemorrhage.

This 9½-year-old boy was admitted to Children's Hospital on May 7, 1947. Prior to entry he had been in excellent health and was normally very bright and active. On the evening before admission he returned home after playing baseball complaining of headache, and vomited. He was put to bed. At 3:00 A.M. his mother was awakened by a disturbance in his room and found the boy lying on the floor

thrashing wildly about, soiled with urine and vomitus.

On admission to the hospital he was wild and delirious. The pupils reacted poorly to light. His neck was slightly stiff. There was bilateral ankle clonus. The preliminary diagnosis was encephalitis or meningitis. Spinal puncture, however, revealed very bloody fluid.

The boy's condition remained precarious for several days. Eye signs were variable and it was felt that subarachnoid hemorrhage was secondary to massive intraventricular bleeding.

With conservative treatment there was painfully slow improvement. During his very stormy course, transient weakness of the right face and arm was noted, along with a right sixth nerve palsy.

On June 26, 1947, a pneumo-encephalogram was done. This demonstrated an air-filled pocket in the left frontal lobe communicating by a very narrow channel with a dilated left lateral ventricle.

At the same time an angiogram was done. The combined air film and angiogram (Figure 4) shows an obvious arteriovenous aneu-

rysm. The carotid artery is seen going up to the anterior cerebral; the anterior cerebral sends several large branches to the central area of flaky, opaque medium, and from this point, coursing rostrally, is a very large dilated vein.

It seemed clear that this aneurysm had ruptured into the left frontal lobe and the hemorrhage in turn had broken into the ventricle. Operation was performed on June 27, 1947, through a left frontal lobe flap. After reflection of the dura, even after the ventricle had been tapped, the left frontal lobe was very tense and bulging. At the extreme medial border was a large vein running rostrally and medially into the longitudinal sinus. It was possible to dissect the frontal away from the falx and to place a clip on the frontopolar branch of the anterior cerebral artery. With the arterial supply of the lesion thus occluded it was a simple matter to resect the medial portion of the frontal lobe with the contained aneurysm and intracerebral hematoma.

Except for an attack of appendicitis during the hospital course, his subsequent course was satisfactory. The boy was discharged on July 24, 1947, four weeks after craniotomy. He has continued perfectly well and is active and alert.

DR. SCHWARTZ: Are you going to school now?

PATIENT: Yes, sir.

DR. SCHWARTZ: Playing baseball?

PATIENT: No, sir.

DR. SCHWARTZ: Are you going to play next spring?

PATIENT: Yes, sir.

This boy has the medial half of his left frontal lobe removed. There is no aphasia because we were able to spare Broca's area.

IN SUMMARY, so-called spontaneous subarachnoid hemorrhage may be said to be a relatively common occurrence. Mortality without treatment is very high. The condition is most commonly due to rupture of an intracranial arterial aneurysm. A diagnosis of congenital aneurysm can be made during life in the vast majority of cases.

Where localization can be made and when the site of the lesion is compatible, direct surgical attack can result in cure. When surgery is not indicated or while awaiting a propitious moment for surgery, conservative treatment stressing complete rest is of great value. In children and young adults the possibility of congenital arteriovenous aneurysm should be borne in mind.

MEDICAL PSYCHOLOGY CURRICULUM PROPOSED

A NEW curriculum leading to a Doctorate in Medical Psychology has been proposed by Dr. Lawrence Kubie, associate in neurology at Columbia University College of Physicians and Surgeons. The proposal was made at a recent two-day conference on "ways to mental health" sponsored by the Harvard Summer School and the Massachusetts Society for Mental Hygiene.

Dr. Kubie believes that such a program would help meet the country's immediate needs for more psychiatrists. He suggests that a pilot test of such training be made by setting up a unit under the joint auspices of a leading medical school and an interdisciplinary university department such as the Department of Social Relations at Harvard.

Students in the proposed training program would be drawn not only from medicine but also from the fields of education, social work, general psychology and others. In contrast to the present training of a specialist in psychoanalytic psychiatry which takes twelve to sixteen years after graduation from college, the proposed new training would take only from six to eight years. Dr. Kubie also pointed out that under this plan existing facilities would be able to train twice as many specialists as at present.

Diagnosis and Treatment of Tularemia

LEE FOSHAY*

UNIVERSITY OF CINCINNATI COLLEGE OF MEDICINE, CINCINNATI

THE DIAGNOSIS of tularemia is seldom too difficult if the seasonal prevalence of the disease and the regional modes of transmission are borne in mind. Although the wild rabbit is the chief source of human infection the colloquial name "rabbit fever" may focus attention too exclusively on this animal as a transmitter.

It is well to remember that *Bacterium tularensis* is widely distributed in nature, that it has relations with approximately 100 wildlife forms, that of these approximately one-half are arthropods, and that of the total about half have transmitted the disease to man. Hence, an essential part of the clinical history of tularemia is contact with a wild animal or contact with a biting arthropod, usually a tick or a fly. Such a history should be sought antecedent to all acute febrile diseases which have an abrupt and severe onset, and which occur during the known period of transmission. Since the incubation period is from one to ten days, usually from two to five, this history, which is so essential and occasionally so easily over-

looked, should reveal an exposure within two to five days prior to the abrupt onset of severe symptoms.

The clinical bubonic types are very easy to recognize. The appearance of a primary lesion and of buboes, or both, within forty-eight to seventy-two hours of an abrupt, severe onset is a very fine leading triad, but the clinical typhoidal type, in which there are no primary lesions or buboes, and in which pneumonia so often dominates the picture, can be at times very misleading. The time and length of the "open season" for tularemia, dependent upon hunting laws, often coincides with the "open season" for pneumococcus, streptococcus, and other bacterial pneumonias. Under these circumstances tularemia may be forgotten. There may also occur combined or multiple infections. In such times it is wise to adopt the rule that when sputum from pneumonic patients does not display gram-positive cocci, or enough bacteria of any kind to excite attention, blood should be taken every three to four days for *Bacterium tularensis* serum agglutination tests.

This same procedure could wisely be followed during the hunting seasons in all instances of abrupt onset, severe, markedly prostrating, acute febrile infections, especially those in which early trials with sulfonamides and penicillin are ineffective.

*Professor of Bacteriology, University of Cincinnati College of Medicine; Director of Service, Cincinnati General Hospital, Cincinnati.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.



LEE FOSHAY

The agglutination test is standard and usually sufficient, a test of amazing reliability. It is never positive during the first week of the disease. It usually becomes positive sometime during the second week, with the titer rising abruptly later in that week or at the beginning of the third week, rising usually to a level of 1:640 or 1:1280.

Once a patient has acquired serum agglutinins as a result of tularemic infection, they persist for the length of life of the patient. This situation is quite unlike that of bacillary dysentery or of typhoid or paratyphoid fevers. The agglutinin titers in tularemia do not disappear after recovery is complete. This means, of course, that a person with symptoms that suggest tularemia of six days' duration but who was found on that day to have an agglutinin titer of 1:320 has an existing infection that is clearly not tularemia. The agglutinin titer must have resulted from a previous tularemic infection, assuming, of course, that the history is

correct and that the onset of disease is accurately known.

INTRADERMAL tests may be performed with dilute suspensions of killed *Bacterium tularensis*. The only virtue of the intradermal test—and, by the way, it suffers from faults common to all the intradermal tests—is that it is positive in 92 per cent of cases during the first seven days of disease when agglutinin tests are invariably negative. It does help in some patients, therefore, to use the intradermal test for early diagnosis at a time when the agglutination test for biologic reasons is simply not available. It requires forty-eight hours for the intradermal test reaction to become positive.

Bacterium tularensis has few antigenic relatives among other agents causing human disease. We do observe some occasional cross-agglutination by the serums of patients with acute brucellosis if the homologous titers are high. In those cases in which I had opportunity to make tests there was no cross skin sensitization. I know of no infection which will produce a falsely positive reaction to a *Bacterium tularensis* intradermal test. It is highly specific but it will fail in 7 or 8 per cent of all patients selected at random during the first seven days of disease. If failure occurs, and if you still think the disease is tularemia, repeat the test at forty-eight-hour intervals. If you do this you will usually foretell the eventual appearance of agglutinins by a day or two with the final, positive reaction on the second, or perhaps third, intradermal test. In this period the first test never sensitizes to make the third positive.

Streptomycin has become an amazingly effective remedy for this infection. The bacteriostatic level of streptomycin for *Bacterium tularensis in vitro* is 0.3 microgram per cc., and some bactericidal levels, the concentrations at which streptomycin kills *Bacterium tularensis in vitro*, are 1 microgram per cc. for a half hour, and 2 micrograms per cc. for eight minutes. These are small amounts to kill all of approximately 3,000,000 highly virulent *Bacterium tularensis* per cc. The use of streptomycin in

DIAGNOSIS AND TREATMENT OF TULAREMIA: FOSHAY

TABLE I
FREQUENCY OF CLINICAL TYPES AND PNEUMONIA IN STREPTOMYCIN TREATED GROUPS COMPARED WITH
UNSELECTED TYPE AND PNEUMONIA FREQUENCIES

CLINICAL TYPES	STREPTOMYCIN TREATED (%)				UNSELECTED (1212)	
	NUMBER OF CASES	TYPE FREQUENCY, PER CENT	NUMBER WITH PNEUMONIA	TYPE PNEUMONIA RATE, PER CENT	TYPE FREQUENCY, PER CENT	TYPE PNEUMONIA RATE, PER CENT
Ulceroglandular	61	73.5	15	24.6	57	15
Oculoglandular	2	2.4	1	50	3	13
Glandular	2	2.4	1	50	2	10
Typhoidal	15	21.7	10	29	8	51
Total	83		33	40		15

experimental tularemia of the highly susceptible and totally nonresistant laboratory animals, such as the rabbit, hamster, guinea pig, and mouse, betrays its amazing therapeutic efficiency. For instance, in the totally nonresistant white mouse the amount of streptomycin that will always spare exactly one-half of all animals challenged with approximately 100 mouse fatal doses, the median effective doses, is 350 micrograms for the 20 gm. mouse, that is, only 17 micrograms per gram to spare one-half of all mice. So, from *in vitro* and *in vivo* experimental work one would suspect that streptomycin should be an agent of high efficacy in human tularemia.

For human administration intramuscular, intermittent injection is used mostly, usually every third or fourth hour. Continuous drip may be given. Where pain locally is not caused, continuous subcutaneous drip is preferable to continuous intravenous drip. The latter may cause thrombophlebitis.

The purity of streptomycin is now reasonably high and early reactions of unfavorable nature are not seen. But even pure streptomycin may have toxic properties for some patients, causing drug fever, rash, nausea, or muscle cramps—the latter not often reported by others, but seen by us in a fair proportion of those who have untoward reactions. The worst response, the one that we hope will not occur, is the appearance of tinnitus and vertigo, indicating involvement of either division of the eighth cranial nerve.

Blood levels obtained during the administration of 50 mg. every three hours range from

4 to 6.5 micrograms per cc., and with 150 mg. administered every three hours they vary from 25 to 32 micrograms per cc., and with 1 gm. per day, by drip, from 12 to 20 micrograms per cc. of blood. Compare these levels with the *in vitro* killing level of streptomycin, 6 micrograms per cc. in one minute.

THE clinical effect of streptomycin administration in patients with tularemia is usually prompt and often dramatic. Characteristically the fever is down by or before the third day unless there are extensive visceral lesions with large exudates, usually pulmonary but perhaps serosal. The malaise, headache, and characteristic mental depression usually disappear within twenty-four hours, the buboes shrink, and the ulcers, if they are present, start healing. Pain in buboes and pain in initial lesions diminishes promptly. The favorable changes are noticeable, and usually strikingly so, within the first day. Early treatment at a time when the primary lesion is a papule prevents its ulceration. A trifle perhaps, but it betrays the amazing effect of streptomycin in this disease, and it prevents much pyogenic secondary infection of ulcerated lesions which in turn contributes significantly to ultimate suppuration of regional buboes.

The overall effects on the disease may be shown by the results obtained in a group of 83 patients, of whom 2 died.

Table 1 shows that the constitution of the treated group is a proper one for comparison with data from untreated patients or from

TABLE 2
COMPARISON OF MEANS FROM CONTROL AND HYPERIMMUNE SERUM TREATED GROUPS WITH AVERAGES
FOR STREPTOMYCIN TREATED GROUP

		UNTREATED N = 542	HYPERIMMUNE SERUM N = 54	STREPTOMYCIN N = 81
Duration of				
Disease	Months	3.78	2.15	1.95
Disability	Months	3.12	1.87	1.96
Adenopathy	Months	3.50	1.78	1.59
Fever	Days	30.6	28.9	26
Bedridden	Days	46.8	23.3	23
Primary lesions	Days	40.6	30.9	24
Day of disease therapy started			17	20
Suppurative adenitis, per cent.		56	26.5	27.7
Mortality, per cent.		6	3.3	2.4
Therapy-to-recovery interval	Days		46	39

patients treated by other agents. The typhoidal clinical type normally has a fatality rate that is three times as high as the rate of the combined bubonic types. The mortality from any clinical type is increased by an increase in the frequency of pneumonia for that type. Since the treated group contained an unusually high incidence of the typhoidal type, and since the pneumonia rates were higher than normal for all types, it is clear that the group is highly selected with respect to severity of the disease and that significant modification of its mortality and morbidity constants could be expected only from an efficient therapeutic agent.

In Table 2 are shown the morbidity constants that are useful in a statistical study of this infection, those for the streptomycin treated group in comparison with those from 542 untreated patients selected at random and those from 54 patients who were treated with hyperimmune serum. Both therapeutic agents modified significantly most of these constants, streptomycin definitely more so than hyperimmune serum even though it was administered three days later in the disease.

The frequency of suppurative adenitis, one of the main causes for prolonged disability, was halved by therapy. This is perhaps all that could be expected from therapy that was initiated as late as the twentieth day of disease. By this time many regional buboes have already undergone partial liquefaction necrosis. The therapy-to-recovery interval is notably less in

the streptomycin treated group. This interval is the time that elapses between administration of a therapeutic agent and the time at which the patient resumes full time work without subsequent disability. Whenever small groups of treated patients with a disease that is highly variable are to be compared it is often a fairer test to use the therapy-to-recovery intervals rather than to use the full list of aspects of morbidity.

A MORE extended comparison of therapy-to-recovery intervals is shown in Figure 1. Much of the history of experimental therapy of tularemia is summarized in this chart. The upper seven lines show that during the years when serum therapy was under trial the mean duration of disease was progressively shortened as the mean day of disease on which therapy was started moved progressively back from the fifth week toward the onset of the disease. Nevertheless, although the duration of disease was shortened to three-fifths of that of the control group, the therapy-to-recovery intervals remained essentially unchanged, at a duration of 56 ± 4 days. It is assumed that this interval represents the time required by the patient for pathologic lesions to heal and for abnormal physiologic changes to revert to normal.

The first break in the constancy of the convalescent period was caused by hyperimmune serum, which was a better bacteriostatic agent

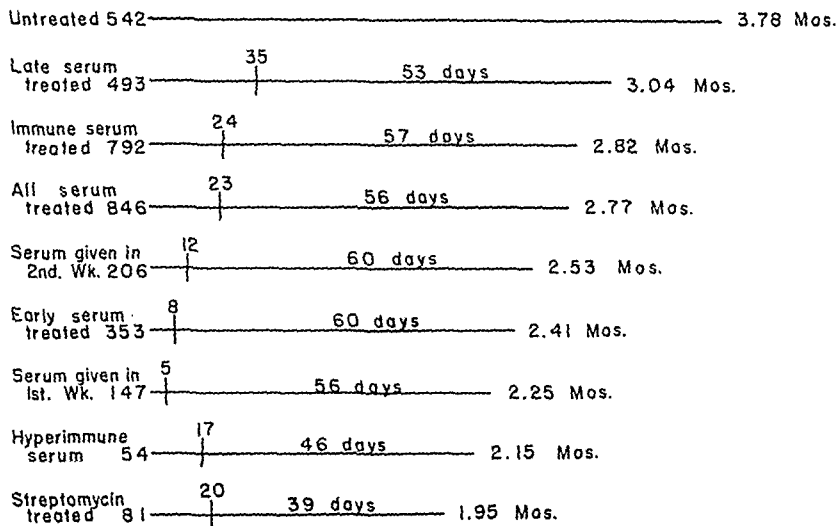


Figure 1. Each line represents the mean duration of disease of its labeled group. The vertical lines and numerals indicate for the treated groups the mean day of disease on which therapy was initiated. The portion of each line that lies to the right of the vertical line represents the therapy-to-recovery interval in days.

than the previously used immune serum. The interval was shortened even though therapy was initiated at the middle of the third week. Streptomycin caused a still greater reduction in the therapy-to-recovery interval and, in addition, reduced the mean duration of disease to less than two months, even though it was first administered at the end of the third week. The much greater efficacy of streptomycin probably indicates that it is not only a much more effective bacteriostatic agent than is hyperimmune serum, but that it is also to some extent bactericidal.

One of the difficulties that may be encountered in the treatment of tularemia patients with streptomycin is traceable to the fact that the treatment is highly effective. This difficulty occurs only when streptomycin is administered to patients with extensive pulmonary or serosal exudates. It does not occur if such lesions are

of small size, or if they are absent. Tularemic exudates, especially pulmonary ones, are heavily laden with actively phagocytic macrophage cells and countless numbers of bacteria. All that is needed to initiate active phagocytosis and digestion of the bacteria is the presence of a highly effective bacteriostatic agent that does not impair the activity of the body cells. This occurs when the streptomycin concentration reaches a bacteriostatic level.

THE consequences of this rapid killing of large numbers of bacteria are either an accentuation of general symptoms of the disease caused by the sudden access of some soluble bacterial products into the circulation, or the analogue of the Herxheimer reaction that is produced by effective treponemacidal therapy when it is administered during a stage of wide

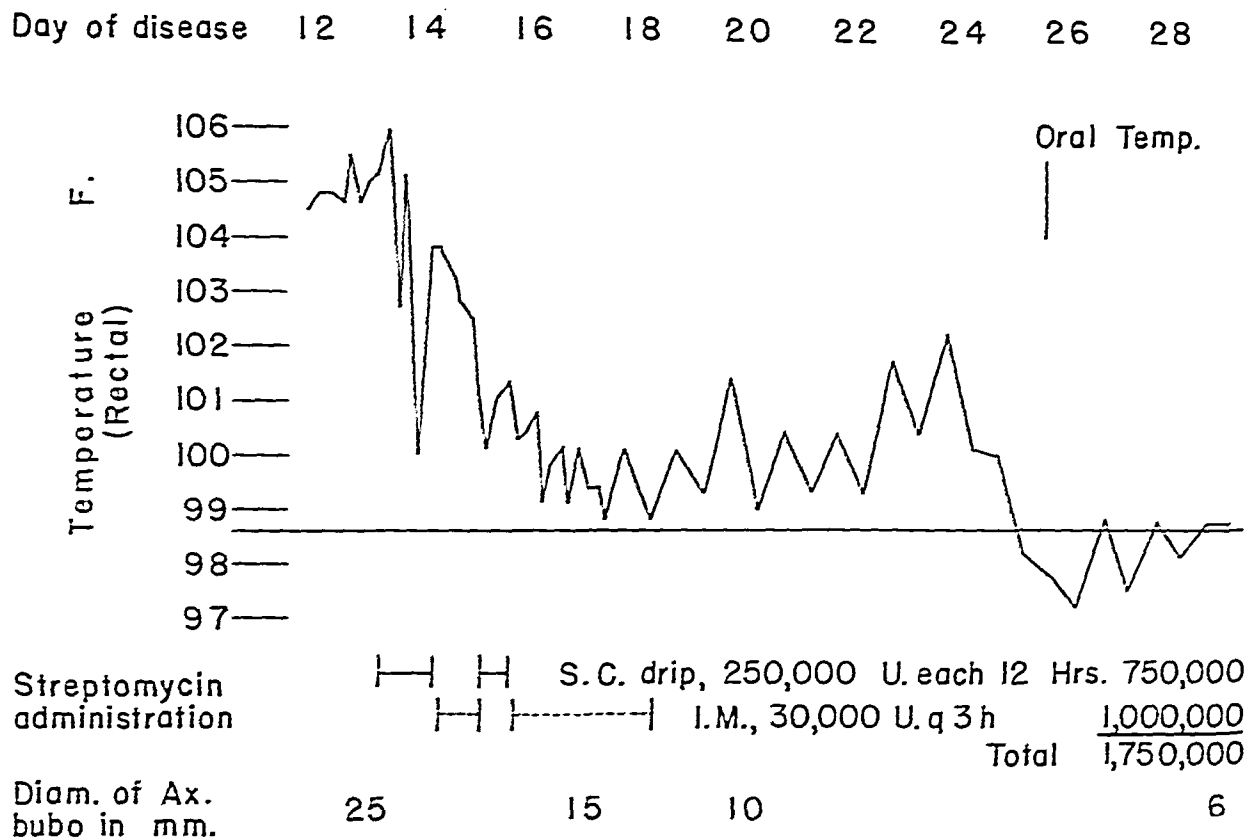


Figure 2. The effect of streptomycin administration on the temperature curve and on the bubo of a desperately ill, comatose man with bilateral tularemic pneumonia. Note the prompt fall in temperature and the shrinkage in size of the node, characteristic features of effective treatment. The recurrent fever, from the seventeenth to the twenty-fifth days of disease, bore no relation to the steady improvement that was observed daily in every other aspect. On the day that the temperature fell abruptly to normal we obtained the first x-ray evidence of resolution of the pulmonary exudates, and it is most probable that this fever was caused by absorption of soluble bacterial products made available by the rapid killing and digestion of the bacteria in the exudates.

(Reprinted with permission from Foshay, L.: A comparative study of the treatment of tularemia with immune serum, hyperimmune serum and streptomycin. *Am. J. Med.* 1:136-138, 1946.)

dissemination of the parasites in the presence of specific antibody formation. In tularemia these reactions have usually consisted of a brief exacerbation of fever, mild constitutional symptoms, a fall in temperature to about normal with a marked amelioration of all symptoms that lasts from four to six days, then a recurrence of irregular fever with daily peaks averaging 102° F. or thereabouts that endures for eight to fourteen days, usually terminating abruptly. This recurrent fever appears after streptomycin administration has been discontinued so there is no question of drug fever, but occasionally it is misinterpreted as a result

of a therapeutic failure, a release from the beneficial effects of streptomycin, and consequently as an indication for additional and energetic streptomycin administration.

In the presence of large infected exudates, such as those of tularemic peritonitis, the exacerbation of constitutional symptoms may be more severe, including higher fever, mental dullness, drowsiness, or even a semicomatose state. There is danger that this type of severe reaction may be misinterpreted as one due to streptomycin toxicity, since it may appear soon after initiation of therapy. The post-therapeutic, recurrent fever cannot be altered in degree

or in duration by any form of therapy, and its disappearance often coincides with the first obtainable evidence of resolution of the large exudate. The most complete available exposition of the cause of this reaction is in the clinical chart of Cohen and Lasser's patient,¹ a desperately ill man with a large tularemic pneumonia. Upon admission this man showed a sustained, nonremittent fever at a high level and disorientation and stupor, a combination that constitutes the worst prognostic sign in tularemia. Careful examination of this chart shows that the dramatic, favorable changes accomplished by streptomycin were all effected at an administration rate of 0.5 gm. per day, and no convincing evidence that subsequent administration at a higher rate added anything of value. It also reveals that coincident with the onset of recurrent fever the serum agglutinin titers fell, indicating clearly an *in vivo* antibody absorption. This could be caused only by the release of a large amount of soluble bacterial antigenic material into the circulation.

The source of so much antigenic material in a person abruptly transferred into the recovery, or antibody, phase of the infection, could only be the bacteria in the large exudate, now subjected to accelerated phagocytosis and digestion as a consequence of streptomycin effect. Drs. Cohen and Lasser correctly interpreted the events and did not give extra streptomycin. Indeed, if attention is focused on the condition of the patient rather than on the clinical chart, it is usual to observe that despite recurrence of fever the patient improves steadily day by day.

Figure 2 illustrates the effect of streptomycin therapy in a desperately ill patient at the Cincinnati General Hospital from whom we tried to learn how much streptomycin is enough. The man was known to have had pneumonia for six days, and had been semicomatose for that period. He had bilateral tularemic pneumonia on admission. Note the sustained high fever during the first two hospital days. We have never observed a spontaneous recovery in any patient with these findings. Streptomycin administered by subcutaneous drip at the rate of 0.5 gm. per day for one day brought the

rectal temperature down from 106° to 100° F. and restored the patient to a somnolent but easily arousable and rational state. The change to intramuscular administration at a rate of slightly less than 0.25 gm. per day caused the temperature to rise again and the patient to lapse into a deep stupor. Reversion to 0.5 gm. per day for just one-half day again rendered him essentially afebrile and mentally rational. From then on resubstitution of intramuscular administration at the rate of 0.24 gm. per day sustained the clinical gains quite satisfactorily.

It is probable that no sicker tularemia patient has been treated successfully, yet you will note that the total amount of streptomycin administered was only 1.75 gm. However, it is conceivable that one might encounter a patient who was farther along toward that point at which all pathologic-physiologic changes become irreversible, and it is possible that a larger dosage of the drug might be necessary.

In the treated series, streptomycin dosage varied from 0.64 to 42 gm. per patient. There is obviously much wasteful use of it. It seems probable that no dosage greater than 6 gm. per patient could be justified by any available experience or knowledge, and that 2 to 3 gm. per patient is probably adequate dosage for the great majority of patients. Certainly there is yet no valid evidence that 0.5 gm. per day for two days, followed by 0.25 per day for four days, a total of 2 gm.; or that 0.5 gm. daily for six days, a total of 3 gm., is not sufficient for most patients. We probably have not had collectively enough experience to justify any hard and fast rules. Nevertheless, since streptomycin in moderate dosage can cause prolonged or permanent tinnitus, vertigo, or deafness, due to the unfortunate vulnerability of the eighth cranial nerve, it would seem wisest to use always the least amount that is wholly adequate for the clinical need.

REFERENCE

- ¹Cohen, R. B., and Lasser, R.: Primary tularemic pneumonia treated with streptomycin. J.A.M.A. 131:1120-27 (August 3) 1946.

Differential Diagnosis and Treatment of Arthritis

RALPH A. KINSELLA*

ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

FIVE YEARS ago I had the pleasure of speaking to this Assembly on the same subject. At that time the treatment of rheumatoid arthritis with gold was being popularized, but there were still a great many uncertainties and disadvantages in the treatment, some of them arising from the enthusiasm with which patients were treated and consequently overtreated. In the five years that have passed considerable experience has been accumulated, and a body of opinion is being formed concerning this method. It is not the perfect treatment. All cases do not respond favorably, but in contrast to the preceding period when no treatment was successful, patients can be assured now that in a large number of cases improvement will take place, and if the patients are treated early enough even permanent remission may be expected.

The etiology of this disease remains obscure. Thinking has changed somewhat so that rheumatoid arthritis is now included in the list of those diseases which are characterized by the alteration and disturbance of collagen. Collagen is a ground substance in connective tis-

sue, and certain kinds of disease entities in which the process of allergy is known or suspected to exist show this alteration of collagen and, subsequently, other surrounding cellular changes differing with the different diseases.

This concept has been adequately elaborated by several writers in the last ten years. Klemperer, Pollack and Beehr have written very clearly about the subject, and the correlation of all these diseases into one concept has been well described by Rich.

A consideration of the different diseases that are included in this classification may give some idea as to the adequacy of certain kinds of treatment. This list includes serum sickness, acute rheumatic fever of the typical variety, and also the rare variety that is not characterized by cardiac disease, lupus erythematosus, periarthritis nodosa, dermatomyositis and psoriasis, fasciitis, and finally rheumatoid arthritis. Here also there may be variants that are not clearly identified.

I should like to dismiss from discussion the great group of cases called osteoarthritis. I think this expression has contributed very little to the understanding of arthritis, and I think it would be just as well if we paid little or no attention to x-ray evidence or x-ray statements about osteoarthritis. You know about the person who comes to a doctor's office with a swab-

*Professor of Internal Medicine and Director of the Department St. Louis University School of Medicine, St. Louis.

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len knee, an x-ray picture reveals spurs, and then the diagnosis of osteoarthritis is made. But if the healthy knee is photographed in the x-ray, the same spurs are seen, and the same spurs are seen all over the body. Thus osteoarthritis is not a disease and it is not an adequate explanation of the illness of patients. It might be in order for the expression to be re-examined and a substitute evolved.

Pains in the back, swollen knees, lame shoulders—all those disturbances which comprise the greatest number of cases in an arthritis clinic usually do not result from arthritis at all but from some orthopedic or mechanical disturbance and should have orthopedic treatment. The bad foot and the bad shoe are much more responsible for bad knees and bad backs than any disease process.

Rheumatoid arthritis is the chief form of chronic arthritis to be discussed because it is the most dangerous and most disabling form. From my experience with these patients and their doctors I feel that it is still necessary to emphasize the features which lead to the diagnosis. I think the word "rheumatoid" ought to be limited to a certain group of patients that have certain definite clinical features. In the first place, the disease occurs early in a person's life. Most of the cases develop rheumatoid arthritis when comparatively young in years, in the twenties or thirties; in childhood the counterpart is Still's disease. Practically every patient who is examined for rheumatoid arthritis for the first time during his fifth decade is found to have had an insidious onset dating back into his twenties or thirties. The disease seems to have a predilection for women. Most of the cases undoubtedly are found in women, but the disease is not uncommon in men.

The mode of onset is different from that of any other kind of chronic arthritis. It is insidious, it is indefinite. A pain may exist in a wrist for months or even years intermittently without exciting much attention or producing enough evidence to yield a positive diagnosis. In other cases the advance of the disease is more definite and rapid, and once a single joint becomes swollen and painful only a few months



RALPH A. KINSELLA

will elapse before many joints are affected in a similar manner.

The disease is definitely not associated with any recognizable disturbance in endocrine function or with any recognized infective process. There is no connection between teeth, tonsils, and sinus and rheumatoid arthritis.

THE DISEASE further characterizes itself by spreading to the smaller joints. In the literature of the last twenty or twenty-five years this fact has been emphasized, and the expression "spindle finger" or "fusiform finger" has been used to describe it. The process characteristically involves the middle knuckle of the finger and spares the last joint of the finger. This gives the finger a swollen middle, or a fusiform or spindle shape. It is a curiously valuable sign for the recognition of this type of rheumatoid arthritis. Other forms of chronic rheumatism may involve the fingers, but they do so in a different way, as I shall point out.

These swellings are what might be called pale cold swellings. They consist of painful, purify areas around the wrist, the middle joint of the finger is swollen, but it is neither red nor hot, and it is tender and painful. You know the rest of the picture—the spreading disability, the pain on movement, the difficulty the patient has in making a living.

The introduction of gold in the treatment of this disease has been extremely valuable. In the beginning gold was used in excessive amounts and many unfavorable results took place. The experience of the last ten years has brought the treatment with gold to a point where it is safe, and complications are extremely rare. This treatment consists of giving gold in 50 mg. doses of a recognized gold salt, such as myochrysin, once a week. This treatment is usually and arbitrarily continued for twenty weeks and then the patient is allowed a rest period. The rest period may have grown out of the fact that in the early days when greater doses were used the patient at the end of twenty weeks would show frightening complications. Now, however, it is thought that, with smaller doses being used, there should not be any real rest period in which no gold is used; instead, the present trend is to give gold every two weeks for two to three months and then to resume the weekly program.

There is no question about the value of this treatment in many cases of rheumatoid arthritis. Not all cases are cured by any means. Experience will differ, depending on the clinic which reports the use of this treatment. For example, if a clinic is in a position to see patients only for a few months and if the treatment cannot be controlled over a long period of time, relapses are so common that it is easy to form the opinion that the treatment may be a total failure in some cases.

I think it is important that even when patients do not seem to improve after a year, the treatment should not be abandoned, because improvement may come at a much later date, even two years after the beginning of treatment. This, of course, has a tendency to weaken the argument for the use of gold, but it is a

fact that some patients, particularly those who have had arthritis for eight to ten years before treatment has started, will be very slow to show improvement. On the other hand, if the patient presents himself within a month or two after the onset of painful swellings in small joints, then some very surprising improvements occur. Undoubtedly the best results are seen in those cases where treatment can be started soon after the onset. However, the average patient, I think, does not present himself for treatment for at least a year after the onset, because of the indefinite and slowly progressive character of the disease.

THE COMPLICATIONS that come from using gold are not as numerous or serious today as they used to be. At the rate at which gold is now used a patient rarely has anything more serious than an itch with a very faint eruption on the flexor surfaces, and this is not a sufficient reason for discontinuing the treatment. Benadryl will relieve this itch. There have been reports in the literature for the last two or three years from some clinics on the effects of BAL, the British anti-lewisite material which was evolved for the treatment of arsenic and mercury poisoning, in those patients in whom more serious complications from the use of gold have developed. In a recent number of the *Annals of Internal Medicine* this subject is reviewed, and it is apparent that in some cases of severe heavy metal poisoning following the use of gold and the use of larger doses of gold, BAL may be effective in completely removing any dangerous threat to the patient.

I have had no opportunity myself in the last two years to see a patient whose complication was serious enough to consider the use of this material, and I think it has been used, in the reports to date, in patients who need not have had any such treatment.

The most remarkable complication that I personally have seen was in a young woman who had had all the clinical features of rheumatoid arthritis for several months before presenting herself. After two injections of 50 mg.

of gold she developed universal adenopathy with a high fever and was hospitalized. She was studied for a possible infectious mononucleosis, a diagnosis that could never be established. After ten days the fever subsided, the enlarged glands returned to normal size, and all the features of rheumatoid arthritis disappeared. She has been free of symptoms for the fourteen months since her discharge from the hospital. If we could unearth the reasons for her recovery, we might develop a treatment for rheumatoid arthritis which is better than gold therapy.

I think there is another form of chronic rheumatism that is important in the practice of all of us. I think you and I see such a patient about once a year. This patient is definitely in the past-middle-age group. The sex is almost always male, about five males to one female in my short series of 15 patients.

The mode of onset is different. It is much more rapid, it is abrupt, and the disability is quick to be established. The large joints, and the hands as well are involved. Many of these cases are called rheumatoid arthritis when in reality they must represent an entirely different process. Some of these patients have had definite infections active in the body at the time. In several of the males, active urinary tract infection was present, but many of the patients had no discoverable infection. Whether or not infection has anything to do with this type of patient is difficult to state.

The difference between the hand of this patient and the hand of the rheumatoid arthritis patient is diagnostic. The rheumatoid arthritis patient has one or more spindle-shaped fingers, interosseous atrophy, and a bulky wrist, whereas the patient with this other kind of prolonged inflammatory rheumatism has a helpless hand that is immobile because the total hand is occupied in a dull red, tender uniform swelling. There is no tendency to localization at any one point, but the entire hand is swollen and slightly reddened. The onset is characterized by fever, and the fever may be as high as 102° in the first week.

These patients may let a long time elapse

before being properly treated; they may wait a year. Some of the patients undoubtedly get well without any particular treatment. The injection of vitamins (which appears to be inevitable), the use of any antibiotic or sulfa drug (also inevitable procedures), may have something to do with the recovery of some of these patients, but such procedures undoubtedly had nothing to do with the recovery of a great many.

TO REVERT for a moment to the classification of those diseases characterized by disturbance of collagen, you will recall that one of the diseases listed was lupus erythematosus, a disease whose history lies in the literature of dermatology. Far back in the literature on that disease two agents were stressed as useful in treatment, gold and bismuth. The emergence at this late date of a classification which places rheumatoid arthritis in a group with lupus erythematosus is doubly interesting since gold has also been developed as one of the treatments of rheumatoid arthritis.

In the other type of case that is clinically different from rheumatoid arthritis, there is no doubt, it seems to me, that bismuth is an extremely valuable agent, and weekly injections of bismuth usually cause an improvement in four or five weeks.

I have had the opportunity of treating two such patients with gold and have had equally beneficial effects. These patients get well, and if added to any one series of rheumatoid arthritis cases would certainly improve statistics. I am not absolutely sure that they would not all get well with a residue of stiffness and some deformity if they had no special treatment whatever, because some of them undoubtedly have done so, but it seems to me that the process of recovery is accelerated, even initiated, by the use of bismuth and possibly, if we knew more about it, by the use of gold.

Finally, one sees at times patients with pains and stiffness who do not fall into one of these common categories, patients who have what might be called fasciitis. These cases are char-

acterized by painful stiffness of the panniculus, the subcutaneous tissue, by contractures of the palmar tendons or of all the tendons, and by tenderness of the flesh when pressed upon. There is no particular tendency toward involvement of the joints.

Such a case suggests both scleroderma and dermatomyositis, particularly if there are skin manifestations; many of these cases resemble scleroderma or dermatomyositis but do not have the superficial manifestations of those two diseases. In two such patients gold has been definitely helpful in relieving the symptoms. Those were not cases called *scleroderma*, for which so far I think we have no real treatment.

Finally a word about the physical examination of the patient. I would like to repeat that it ought to be a routine practice of doctors to examine patients from the feet up instead of from the head down. Instead of the ordinary routine that you see of taking out the light and looking at the pupils, every patient should disrobe, in-

cluding shoes and socks, and the examination begun at the feet, not only for the purpose of examining the arteries of the feet, which is extremely important, but also for the purpose of examining the feet, the bones, and the posture of the foot itself. In that way I believe we could recognize the origin of many complaints referable to joints that are called arthritis. Painful and swollen knees, pain in the neighborhood of the groin radiating to the back of the iliac crest, pains in the area of the sacroiliac, pains as high as the base of the skull, all these might at times be explained on the basis of faulty weight-bearing and identified much more often if the doctor used the routine method of beginning his physical examination at the feet. It is a practice that will repay you many times in satisfactory diagnoses and highly satisfactory treatment, because corrective measures in the shape of shoes or orthopedic correction will bring about recovery of these patients in many instances.

NAVAL AIR RESERVE NEEDS DOCTORS

DOCTORS who served in the Navy during the past war and who still hold reserve commissions are requested to apply for two-weeks annual training duty or up to five months extended duty at Naval Air Stations, it was announced by Rear Admiral Richard F. Whitehead, USN, Chief of Naval Air Reserve Training.

Naval Reserve Medical Officers who can possibly spare the time are urged to apply for this duty to help alleviate the work-load at those stations which are under-manned. Applications are made via the Commanding Officer of the Air Station to the Commandant of the Naval District concerned. The following Naval Air Stations need assistance: NAS Akron, NAS Atlanta, NAS Columbus, NAS Dallas, NAS Denver, NAS Glenview, NAS Grosse Ile, NAS Los Alamitos, NAS Memphis, NAS Miami, NAS Minneapolis, NAS New Orleans, NAS New York, NAS Oakland, NAS Olathe, NAS Squantum, NAS St. Louis, NAS Willow Grove, NAResTraUnit, Anacostia, D.C., NAResTraUnit, Jacksonville, NAResTraUnit, Norfolk, NAResTraUnit, Seattle, NAResTraUnit, Lakehurst.

Congenital Anomalies
of the
Heart and Great Vessels

*Clinicopathologic Study
of 132 Cases*

Part II

T. J. Dry • J. E. Edwards • R. L. Parker
H. B. Burchell • H. M. Rogers
and
A. H. Bulbulian

MAYO CLINIC
ROCHESTER, MINNESOTA

FOREWORD

The Editors of *Postgraduate Medicine* are pleased to present the second and concluding installment of the exhibit on Congenital Anomalies of the Heart, of which Part I appeared in the September issue of this journal.

Originally shown at the centennial meeting of the American Medical Association in Atlantic City in June, 1947, the exhibit has been amplified by the addition of reproductions of portraits of pioneer investigators in the field of congenital heart disease. The authors have also studied additional cases and have modified their data in respect to the incidence of the various types of anomalies accordingly. Apart from these additions and changes, the material presented here is essentially that included in the original exhibit.

For the sake of completeness, the authors would like to have included a presentation of such anomalies as congenital subaortic stenosis, anomalous opening of the pulmonary veins into the right auricle and an anomalous origin of a coronary artery. Specimens of such anomalies, however, were not available in their pathologic material.

Tetralogy of Fallot

*(Pulmonary Stenosis, with Narrow Pulmonary Artery,
Ventricular Septal Defect and Dextroposition of Aorta)*

ETIENNE-LOUIS ARTHUR FALLOT

1850-1911



In 1888 Fallot wrote "Until now clinicians have considered the diagnosis of anatomic lesions of morbus caeruleus of almost unsurmountable difficulty." Although the combination of lesions known as the "tetralogy of Fallot" had been recognized as an anatomic entity more than 100 years before, it took the next 50 years for the medical profession to appreciate the fact that this meticulous physician had paved the way for the accurate selection of cyanotic patients who might, years later, be benefited through surgical intervention.

Tetralogy of Fallot

*(Pulmonary Stenosis, with Narrow Pulmonary Artery,
Ventricular Septal Defect and Dextroposition of Aorta)*

IN THIS heart the aorta arises from both ventricles and straddles a defect of the membranous portion of the ventricular septum. In contrast to the dilatation of the pulmonary artery in the Eisenmenger complex, the pulmonary artery in this condition is narrow, and there is a stenotic subpulmonic "third ventricle." The right ventricular wall is thick.



Fig. 41—Anterior view (model x1).
(1) Narrow pulmonary artery. (2) Wide aorta.
(3) Large right ventricle.



Fig. 42—Interior of right ventricle (model x1).
(1) Narrow pulmonary artery. (2) Subpulmonic "third
ventricle." (3) Ventricular septal defect.

History of the Patient

BOY, 7 years old with increasing cyanosis since three days after birth, and very limited tolerance of exercise. Intense cyanosis, clubbing of fingers and toes, and a soft precordial systolic murmur were present. Roentgenogram showed heart not enlarged, with classic concavity of left border. Hilar markings prominent, but no hilar pulsation noted roentgenoscopically. Marked right axis deviation. Hemoglobin, 24 gm. per 100 cc. blood; erythrocytes, 8,800,000 per cu. mm.; hematocrit, 86 per cent; arterial oxygen saturation, 65 per cent.

Principal Clinical Features of this Anomaly

1. Early cyanosis (low oxygen saturation of hemoglobin in arterial blood). 2. Paroxysmal unconsciousness, with dyspnea and cyanosis, a prominent feature in some cases. 3. Usually, a systolic murmur varying markedly in intensity from case to case. 4. Clubbing of fingers and toes and polycythemia. 5. Subnormal pulmonary arterial flow. 6. Abscess of brain or cere-

brovascular thrombosis occasionally the cause of death. 7. Roentgenologic aspects: usually, heart is not enlarged; pulmonary conus shadow is absent, right ventricle is prominent and hilar pulsations absent. Right aortic arch not infrequently found. 8. Electrocardiogram: marked right axis deviation.

Incidence in this Series—Eleven patients; ages ranged from 22 days to 23 years.



Fig. 43—Interior of the right ventricle. Specimen from which models shown in figures 41 and 42 were prepared.

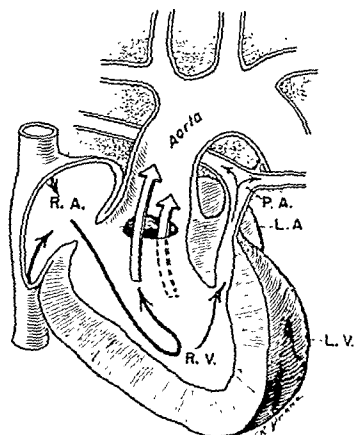


Fig. 44—Diagram of intracardiac circulation in tetralogy of Fallot.

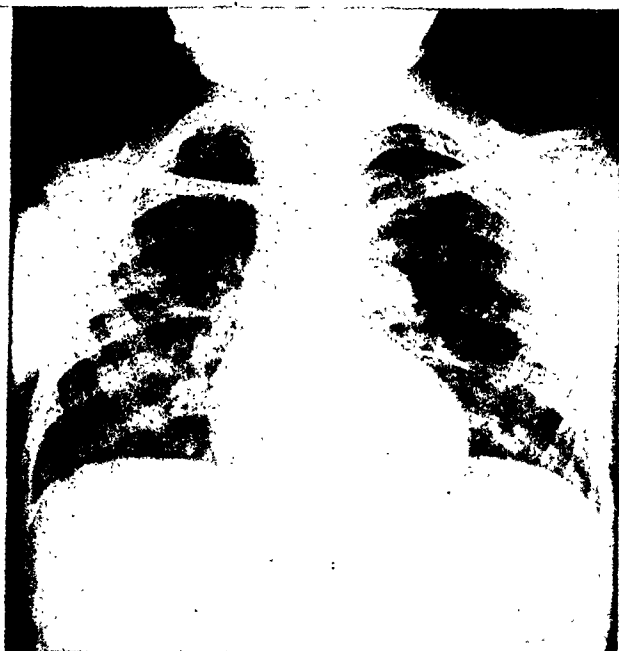
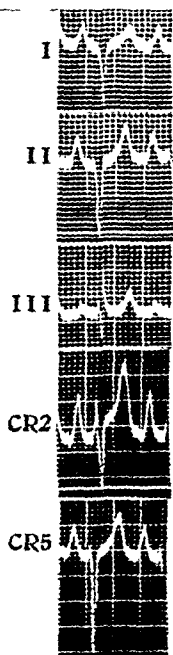
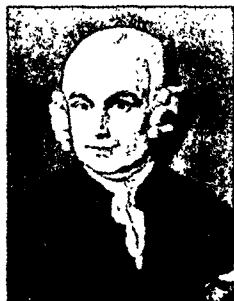


Fig. 45—Electrocardiogram and thoracic roentgenogram of the patient whose heart is illustrated in figures 41, 42, 43 and 44.

Tetralogy of Fallot

*(Pulmonary Stenosis with Relatively Wide Pulmonary Artery,
Ventricular Septal Defect with Dextroposition of Aorta)*



EDUARD SANDIFORT

1742-1814

Eduard Sandifort, professor of surgery, anatomy and medicine at the University of Leyden in the late eighteenth century, is known as the father of pathologic iconography. He has given a very clear description of the cardiac defects now known as the "tetralogy of Fallot." His classic description of how the finger placed in the right ventricle readily appeared in the aorta should be employed as a standard demonstration in pathologic anatomy. Niels Stensen's anatomic description, however, antedated that of Sandifort by about 100 years.

Tetralogy of Fallot

*(Pulmonary Stenosis with Relatively Wide Pulmonary Artery,
Ventricular Septal Defect with Dextroposition of Aorta)*

THIS heart is also the example of the tetralogy of Fallot, in spite of the relatively wide pulmonary artery, since there is stenosis at the level of the bicuspid pulmonary valve. A "third ventricle" is also present which contributes to pulmonary stenosis.



Fig. 46—Anterior view (model x1).
(1) Pulmonary artery. (2) Large right ventricle.



Fig. 47—Interior view of right ventricle and pulmonary artery (model x1).
(1) Stenotic bicuspid pulmonary valve. (2) Subpulmonic "third ventricle." (3) Ventricular septal defect.

History of the Patient

A BOY, 5 years old, of normal development, with progressive cyanosis since 3 years of age. Clubbing and mild polycythemia, as well as a loud precordial systolic murmur with thrill, were noted. Roentgenogram showed heart to be of normal size and contour, but decreased hilar markings. Electrocardiogram showed right axis deviation. The boy died of abscess of the brain.

Principal Clinical Features of this Anomaly (see p. 36.) These two examples, although they differ structurally and roentgenographically in regard to the size of the pulmonary arteries are, nevertheless, identical functionally. The caliber of the pulmonary artery may vary from moderate narrowing to atresia. When valvular stenosis is present, the pulmonary artery and the outflow tract may approach that of a normal heart, and it is this type of stenosis that may be associated with an intact ventricular septum and absence of cyanosis. Variation is found in the length of the subpulmonic, fibromuscular channel sometimes called the "third ventricle." This channel may be narrow throughout its length or it may exhibit stricture-like contractions at either end. The clinical features are largely dependent upon the reduced pulmonary blood flow. When the syndrome is associated with a right aortic arch, it has sometimes been called "Corvisart's disease." Wide bronchial arteries may carry a substantial amount of blood to the lungs in this condition.



Fig. 48—Interior of the right ventricle. Specimen from which models in figures 46 and 47 were prepared.



Fig. 49a—A stenotic bicuspid pulmonary valve in a case of tetralogy of Fallot; b—wide bronchial arteries in a case of tetralogy of Fallot.

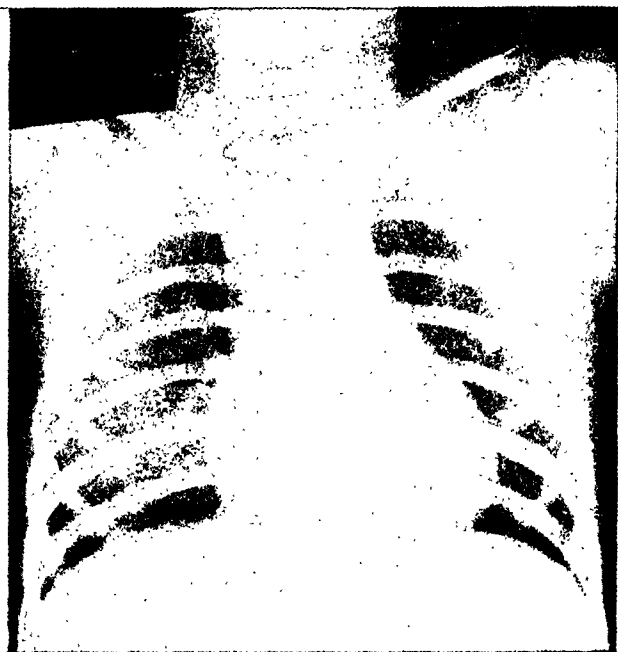
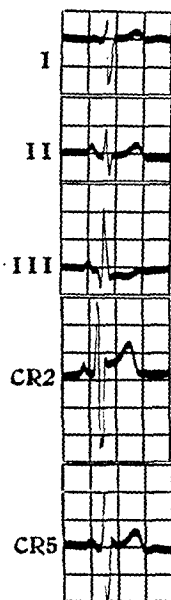


Fig. 50—Electrocardiogram and thoracic roentgenogram of the patient whose heart is illustrated in figures 46, 47 and 48.

Complete Transposition of the Great Vessels



KARL ROKITANSKY

1804-1878

In Rokitsansky's study, "Die Defekte der Scheidewände des Herzens," 1875, the anomalies of the great vessels, the defects of the atrial and ventricular septa and the theories relative to the etiology of transposition are described. The illustrations of the various lesions are detailed and beautifully executed, and the engraving of the anatomic defects in what we call tetralogy of Fallot is especially excellent. In his study of the great vessels, published in 1852, the cases of patent ductus arteriosus have an excellent clinicopathologic correlation, the clinical findings often being those of his contemporary and friend, Skoda.

Complete Transposition of the Great Vessels

IN THIS anomaly the aorta arises from the right ventricle and the pulmonary artery from the left ventricle. A defect of the membranous portion of the ventricular septum is present in this specimen. The foramen ovale and the ductus arteriosus are patent.



Fig. 51—Anterior view (model x1).
(1) Aorta situated anterior to (2) pulmonary artery.

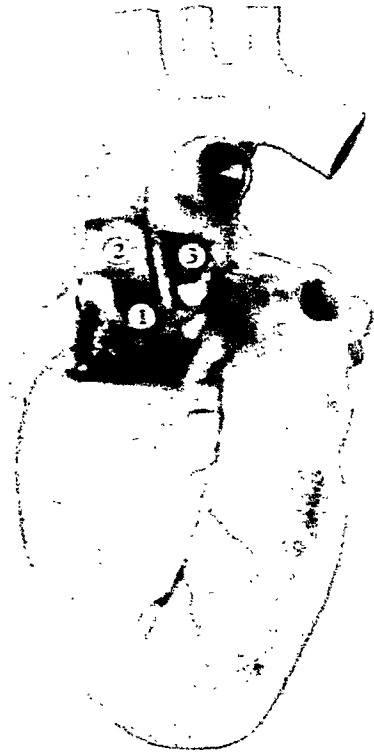


Fig. 52—Left lateral view (model x1).
(1) Ventricular septal defect. (2) Aorta arising from right ventricle. (3) Pulmonary artery arising from left ventricle.

History of the Patient

A FEMALE, 2 months old, had had intense cyanosis at birth, which disappeared. Intermittent cyanosis recurred at 5 weeks. The patient was hospitalized for "pneumonia" at 2 months. Cyanosis and dyspnea increased, with evidence of congestive heart failure. A systolic murmur over the precordium and interscapular area was noted. Roentgenograms of the thorax showed globular cardiac enlargement, with abnormally narrow shadows of the great vessels in this plane. Electrocardiogram showed high voltage biphasic QRS complexes. Progressive respiratory embarrassment and death ensued.

Principal Clinical Features of the Anomaly

1. Cyanosis, onset at birth, severe and progressive.
2. Usually, death in early infancy, condition not compatible with adult life.
3. Progressive cardiac enlargement.
4. Variable systolic murmur.
5. Roentgenologic aspects: usually, right ventricular enlargement, globular configuration, aorta anterior to pulmonary trunk.
6. Electrocardiogram: usually, right axis deviation; occasionally, left axis deviation.

Incidence in this Series

Nine patients, of whom 7 did not survive beyond the fourth month. One survived to the age of 7 months; 1 other to the age of 8 months.



Fig. 53—Specimen from which models shown in figures 51 and 52 were prepared. Interior of the right ventricle and aorta.

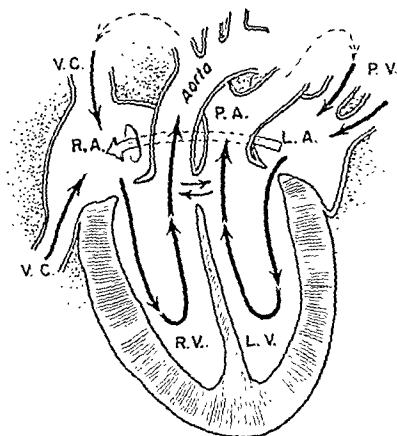


Fig. 54—Diagram of intracardiac circulation in complete transposition of great vessels with ventricular septal defect.

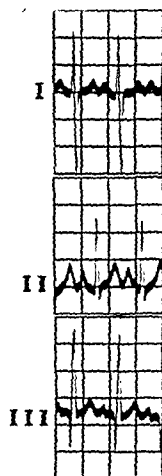
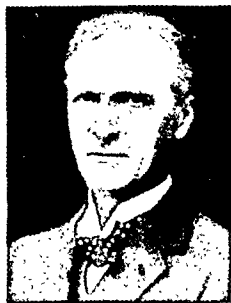


Fig. 55—Electrocardiogram and thoracic roentgenogram of the patient whose heart is illustrated in figures 51, 52, 53 54.

Persistent Truncus Arteriosus



SIR ARTHUR KEITH

1866-

For many years Sir Arthur Keith pursued his studies on congenital cardiac disease, mainly from the embryologic viewpoint. His contributions to knowledge of the embryologic defects of the heart largely concern his observations on the normal and abnormal differentiation of the bulbus cordis. However, his researches were wide, encompassing anatomic and physiologic correlations. His descriptions of large bronchial vessels in a case of severe pulmonary stenosis are of special clinical interest.

Persistent Truncus Arteriosus

IN THIS heart a single arterial vessel, the persistent truncus arteriosus, arises from both ventricles, above a ventricular septal defect. An incomplete septum divides the upper portion of the truncus arteriosus into the aorta and a short pulmonary artery. No vestige of the ductus arteriosus is present in this specimen.



Fig. 56—Anterior view (model x1).
(1) Persistent truncus arteriosus. (2) Large right ventricle.



Fig. 57—Interior of truncus arteriosus and right ventricle (model x1).
(1) Incomplete truncus septum. (2) Ventricular septal defect below biventricular origin of persistent truncus arteriosus.

History of the Patient

IN A MALE, 8 months old, a systolic murmur was present after birth. There was feeding difficulty, with poor development. The patient was admitted one day before death. A loud systolic murmur was heard over the entire precordium; dyspnea and swelling of the hands and feet were noted; the liver was palpable but there was no cyanosis. The thoracic roentgenogram showed marked cardiac enlargement, with a narrow vascular shadow. The electrocardiogram showed right axis deviation. The infant died suddenly.

Principal Clinical Features of the Anomaly

1. Cyanosis, usually moderately severe, but occasionally absent. Oxygen saturation of arterial hemoglobin always below normal, the degree of desaturation depending on pulmonary blood flow and perhaps the effect, in some cases, of directional ejection from the ventricles.
2. Loud systolic murmur (ventricular septal defect).
3. Roentgenologic aspects: right and left ventricular enlargement. Increased pulsation of hilar shadows may be present, particularly when cyanosis is minimal.
4. Electrocardiogram: usually right axis deviation.

Incidence in this Series—Three patients; the oldest was 8 months of age.



Fig. 58—Specimen from which models shown in figures 56 and 57 were prepared. Interior of right ventricle and persistent truncus arteriosus.

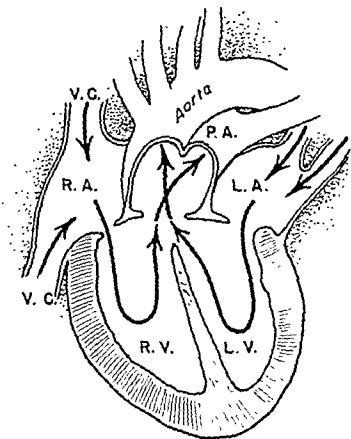


Fig. 59—Diagram of intracardiac circulation in persistent truncus arteriosus.

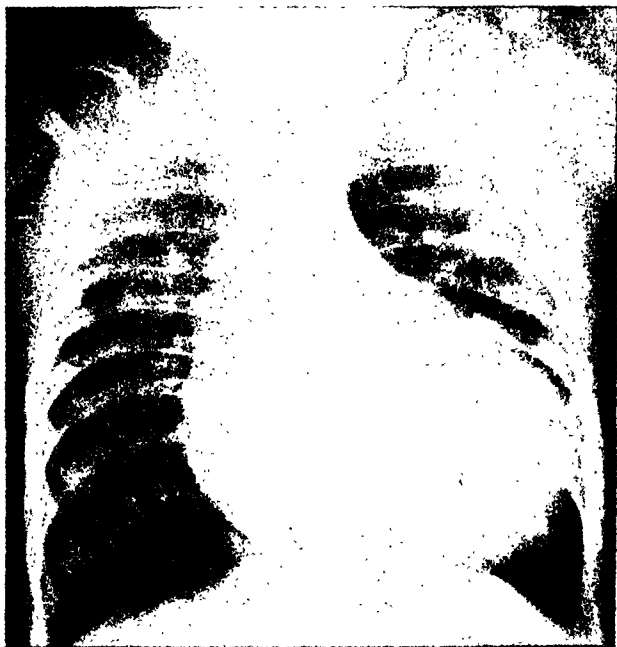
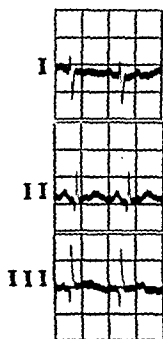


Fig. 60—Electrocardiogram and thoracic roentgenogram of the patient whose heart is illustrated in figures 56, 57, 58 and 59.

Patent Ductus Arteriosus

(*Cylindric and Window Types*)



G. A. GIBSON

1854-1913

In Britain the characteristic murmur of a patent ductus arteriosus is still known as "Gibson's murmur." His repeated emphasis upon the clinical diagnosis through recognition of the characteristic murmur, as well as the physiologic disturbance created by it, were major contributions. His article entitled "Persistence of the arterial duct and its diagnosis," published in 1900, is a classic. Shortly thereafter (1907), an American surgeon, John C. Munro (1858-1910), prophetically referred to the possibility of ligation of a patent ductus arteriosus provided a diagnosis could be made beforehand.

Patent Ductus Arteriosus

(*Cylindric and Window Types*)

THESE two hearts illustrate two anatomic types of patent ductus arteriosus, the cylindric type and the window type. As a consequence of the shunt from aorta to the pulmonary arterial system, there is dilatation of the pulmonary arteries and the left side of the heart.



Fig. 61—Cylindric type (model x1).

(1) Patent ductus arteriosus. (2) Dilated right ventricular outlet.



Fig. 62—Window type (half-size model).

(1) Window type patent ductus arteriosus. (2) Dilated right ventricular outlet. (3) Dilated left pulmonary artery.

History of these Patients

A MALE, 6 weeks old (fig. 61), had had a basal systolic murmur and cardiac enlargement since birth (premature), with feeding difficulty and poor development. Sudden respiratory embarrassment with terminal cyanosis occurred. In a man, 45 years old (fig. 62), a continuous murmur had been heard when he was 30 years old. Cardiac failure recurred intermittently for three years; he died suddenly of pulmonary embolism. On his last admission a loud systolic apical murmur (typical ductus murmur absent) and auricular fibrillation were noted. Systolic blood pressure was 110; diastolic, 70. A thoracic roentgenogram showed cardiac enlargement with a prominent pulmonary artery. Electrocardiograms showed a change to right axis deviation.

Principal Clinical Features of this Anomaly

1. Continuous arteriovenous fistula type of murmur, usually associated with thrill.
2. No cyanosis; normal arterial oxygen saturation.
3. Increased pulse pressure (collapsing pulse).
4. Increased oxygen content of pulmonary arterial blood relative to right ventricular blood (catheter technic).
5. Roentgenologic aspects: prominent left ventricle and pulmonary artery; increased hilar pulsations.
6. Electrocardiogram: normal or left axis deviation.

Incidence in this Series—Twenty patients; 6 weeks to 59 years old. Eight were 35 years of age or older.



Fig. 63—Specimen from which the model shown in figure 61 was prepared.



Fig. 64—Specimen from which model shown in figure 62 was prepared. Interior of the left pulmonary artery. Mouth of ductus in circle.

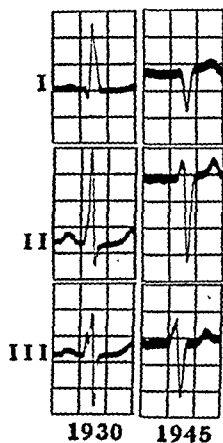


Fig. 65—Electrocardiogram and thoracic roentgenogram of the patient whose heart and great vessels are shown in figures 62 and 64.

Atresia of Aortic Orifice

(Functional Two-chambered Heart)



JULIUS TANDLER

1869-1936

Julius Tandler was the author of many works on gross anatomy as a pure science and on anatomy as applicable to the surgeon. By close association with clinicians, anatomy was for him a science of functioning organs. To the field of congenital cardiac disease, his greatest contributions were the results of his investigations on cardiac embryology. His chapter on the development of the heart in Keibel and Mall's text on human embryology, published in the early part of this century, is still a valuable and authoritative reference.

Atresia of Aortic Orifice

(Functional Two-chambered Heart)

IN THIS heart the primary malformation is atresia of the aortic orifice.

As a consequence of the abnormal circulation, the ductus arteriosus and the foramen ovale are patent, and the right atrium, right ventricle and pulmonary artery are enlarged. The left ventricular wall is thick, but its chamber is diminutive.

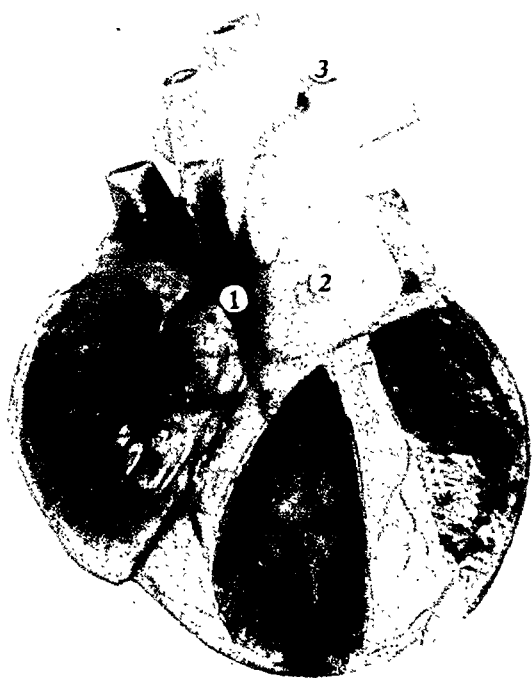


Fig. 66—Anterior view (model x1).

(1) Site of atretic aortic orifice. (2) Dilated pulmonary artery.
(3) Patent ductus arteriosus.



Fig. 67—Left anterior view (model x1).

(1) Diminutive left ventricular chamber.
(2) Thick left ventricular wall.

History of the Patient

IN A FEMALE, 3½ months old, intermittent cyanosis, occurring with crying and exertion, began at the age of 2 weeks. The infant did not gain weight. Dyspnea and cyanosis became more intense. A short basal systolic murmur was present. Hemoglobin amounted to 19 gm. per 100 cc. of blood; erythrocytes numbered 5,670,000 per cubic millimeter of blood. Thoracic roentgenogram showed right ventricular enlargement, with prominent pulmonary conus shadow. Electrocardiogram showed right axis deviation. The infant died suddenly.

Principal Clinical Features of this Anomaly

1. Progressively severe cyanosis.
2. Death in early infancy.

3. Roentgenologic aspects: prominent right ventricle and pulmonary artery.

Incidence in this Series

Seven patients, of whom 5 succumbed by the eighth day. The oldest patient was 3½ months of age.

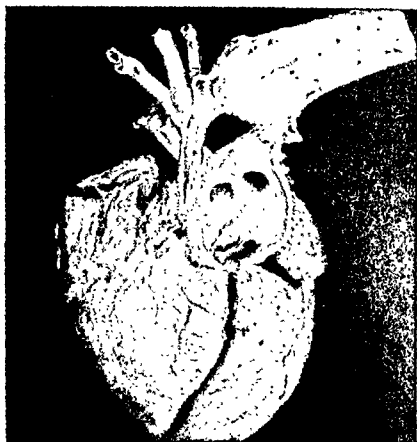


Fig. 68—Specimen from which models shown in figures 66 and 67 were prepared. Interior of pulmonary artery, ductus arteriosus and aorta.

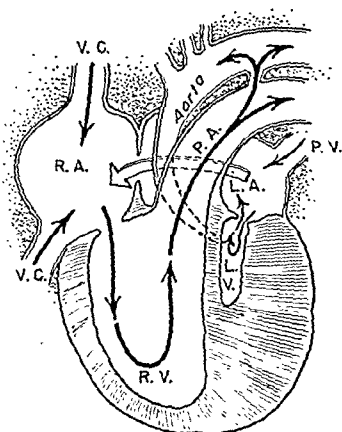


Fig. 69—Diagram of intracardiac circulation in atresia of aortic orifice.

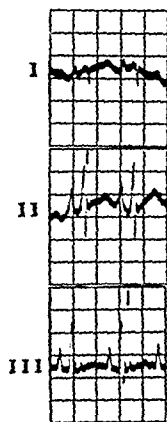


Fig. 70—Electrocardiogram and thoracic roentgenogram of the patient whose heart is shown in figures 66, 67, 68 and 69.

Anomalous Aorta

(With Right Descending Aorta and Right Ligamentum Arteriosum)



JOHN BAPTIST MORGAGNI

1682-1771

In both old and recent reviews, the description of the cyanotic girl of 16 years, in whom Morgagni found a pulmonary stenosis, is considered to be the first good clinicopathologic study of cyanotic congenital cardiac disease. It is of unusual interest because the patient had a relatively rare lesion; namely, pulmonary stenosis without a ventricular septal defect. In spite of the rarity of the lesion, it was the first type of congenital cyanotic lesion correctly diagnosed clinically (James Hope, 1830), and is well illustrated by Peacock (1866).

Anomalous Aorta

(With Right Descending Aorta and Right Ligamentum Arteriosum)

THIS is a rare type of anomalous aorta. It is the mirror image of a more common type of anomaly in which the aortic arch passes over the right bronchus and then behind the esophagus to join the left-sided descending aorta. In this specimen the aorta passes over the left bronchus and then courses to the right, behind the esophagus, to join the descending aorta, which is on the right side. The ligamentum arteriosum is on the right, extending from the right pulmonary artery to the aorta. The right subclavian artery arises from the aorta at the junction of the aortic arch and descending aorta. There is no intracardiac anomaly.



Fig. 71—Anterior view (model x1).
(1) Aortic arch. (2) Trachea and esophagus.
(3) Pulmonary artery.



Fig. 72—Viewed from above (model x1).
(1) Trachea and esophagus encircled and compressed by vascular ring. (2) Right-sided descending aorta. (3) Right-sided ligamentum arteriosum.

History of the Patient

A MALE, 17 months old, had had an imperforate anus at birth; colostomy performed, but development was poor. Dysphagia noted after first year. The infant died of intestinal obstruction.

Principal Clinical Features of these Anomalies

1. Dysphagia (dysphagia lusoria) may or may not be present.
2. In infants: may be marked respiratory distress, with stridor and inspiratory collapse of lower thorax.
3. In adults: extrinsic pulsating lesion has been seen posteriorly by the esophagoscope.
4. Roentgenoscopic examination reveals evidence of right aortic arch or anomalous subclavian artery or double aortic arch.
5. Usually, there is no evidence of intracardiac anomaly.

Incidence in this Series—Two patients: one 2 months old (double arch); one 17 months old.

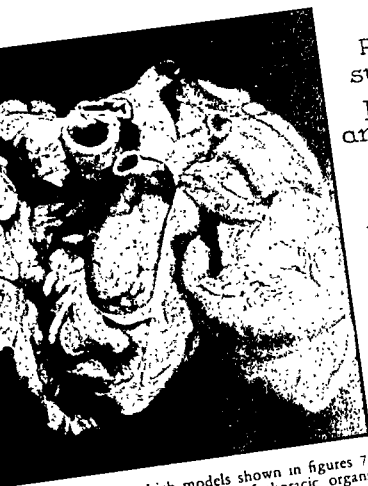


Fig. 73—Specimen from which models shown in figures 71 and 72 were prepared. Superior view of thoracic organs.

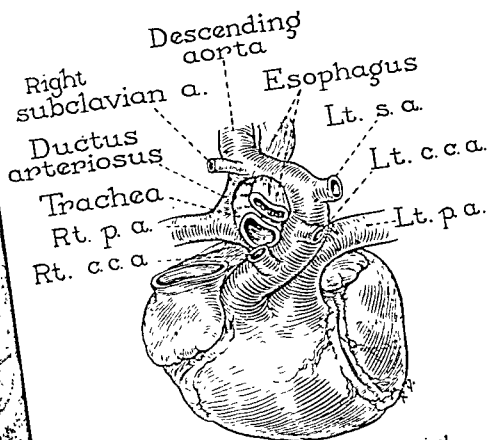


Fig. 74—Drawing of the heart and mediastinal structures in figures 71, 72 and 73.



Fig. 75—Anteroposterior and lateral thoracic roentgenograms in a case of anomalous aorta (right aortic arch).

Coarctation of the Aorta



MAUDE E. ABBOTT

1869-1940

To this century's students of congenital cardiac disease, particularly on the North American continent, Maude Abbott's name justly comes first to mind. Stimulated through an early association with Sir William Osler, she in turn stimulated more extensive interest in congenital cardiac defects and their correlation with the clinical features. Her eminence as a pathologist was widely recognized and her Atlas will long remain an authoritative source of data for studies on congenital cardiac disease.

Coarctation of the Aorta

TWO instances of coarctation of the aorta are shown here. One is an example of a typical "infantile" type of coarctation in which the region of constriction is proximal to a patent ductus arteriosus. In the other, the constriction is in an atypical position, between the origins of the left subclavian and the left common carotid arteries.



Fig. 76—Infantile type (model x1).
(1) Site of aortic coarctation. (2) Patent ductus arteriosus.



Fig. 77—Atypical type in adult (half-size model).
(1) Site of aortic coarctation. (2) Left subclavian artery. (3) Ligamentum arteriosum.

History of these Patients

A MALE, 3 days old (fig. 76), apparently was normal at birth, but on the third postnatal day became cyanotic and died suddenly. A man 26 years old (fig. 77) was admitted with heart failure. Aortic systolic and diastolic murmurs and cardiac enlargement were found. Blood pressure in the right arm was 210 systolic and 40 diastolic; in the left arm it was 110 systolic and 78 diastolic. It was not obtainable in the legs. Pulse was absent in the abdominal aorta and femoral arteries. A thoracic roentgenogram showed cardiac enlargement and absence of the aortic knob, but no notching of ribs. Patient died of aortic valve bacterial endocarditis.

Principal Clinical Features of this Anomaly

1. Hypertension as measured in arms; hypotension or normotension in legs.
2. Decreased or absent pulsation of the abdominal aorta and of the arteries in legs.
3. Palpable pulsating collateral vessels.
4. Frequently, basal systolic murmur; rarely, an aortic diastolic murmur.
5. Roentgenologic aspects: notching of ribs, left ventricular hypertrophy, absence of aortic knob.
6. Electrocardiogram: left axis deviation or left ventricular strain pattern.

Incidence in this Series—Sixteen patients; 3 days to 51 years old (twelve 13 years old or more).

CONGENITAL ANOMALIES OF THE HEART AND GREAT VESSELS

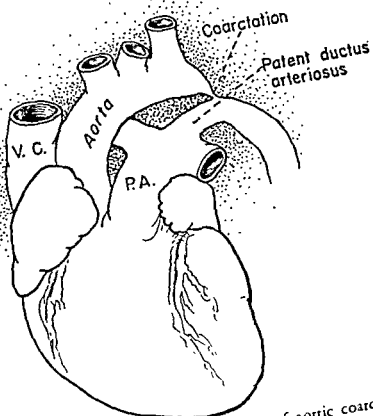


Fig. 78—Diagram of "infantile" type of aortic coarctation.

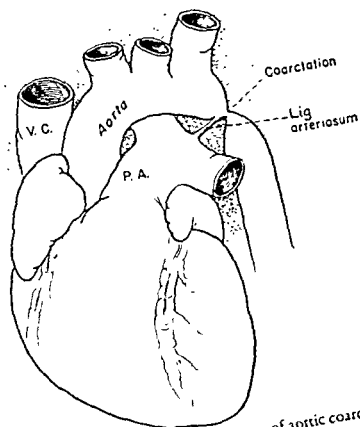


Fig. 79—Diagram of typical "adult" type of aortic coarctation.

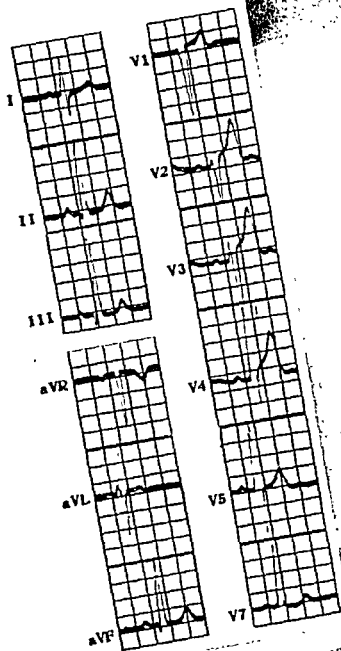


Fig. 80—Electrocardiogram and thoracic roentgenogram in a typical instance of aortic coarctation in an adult.



The Medical Bookman

DIAGNOSIS IN GYNAECOLOGY*

IN THIS new textbook Dr. James V. Ricci has presented in a novel manner, the essential information necessary for correct diagnosis of gynecologic diseases. Instead of describing each disease as a separate entity, the etiology, symptoms, and means of diagnosis are discussed separately for each anatomic division of the female generative organs.

The aim of the text as stated in the preface is to teach the art of gynecologic history taking and the conducting of a careful gynecologic examination in order to arrive at a correct diagnosis. Much of the subject matter presented is based on clinical demonstrations given by the author to student sections of the New York Medical College. Dr. Ricci is clinical professor of gynecology and obstetrics and is also director of gynecology at the City Hospital, New York. In addition he is known for his contributions to literature, particularly his excellent monograph on extraperitoneal cesarean section, and his historical review entitled "Genealogy of Gynecology."

The first part of the text appropriately deals with the basic knowledge necessary before approaching the gynecologic patient. The first two chapters include brief but lucid descriptions of the anatomy, histology, and embryology of the genital structures and their adjacent organs, and a discussion of the source, chemistry, and function of the female sex hormones, including the physiology of ovulation and menstruation. Following is a chapter dealing with general considerations in which the author

describes diagnosis as a matter of analysis and synthesis of data obtained from history, examination, and laboratory data.

Frequently, in intrapelvic disease facts are not available and assumption must be woven into diagnostic thinking. However the author warns that too many assumptions and too few facts lead to a large number of diagnostic errors. The author mentions the large number of female patients who come to the gynecologist with nongynecologic maladies such as neuroses, psychic disturbances, postural and occupational pelvic strains and even nutritional disturbances. The failure of the text to expand to the discussion of psychosomatic symptoms may be explained by the author's assertion that the soundest diagnostician is one who resorts to the diagnosis of neurosis in the fewest cases.

The perfectly written history is stated to be a systematic chronologic record of all the pertinent facts, carefully considered and properly evaluated. It is necessary to gauge the temperament and mentality of a patient, allow her to tell her own story, and use tact and guidance to bring order to the recital. The marital history and menstrual history must be taken in detail with particular attention to the date of the patient's last normal menstrual period since this may be a clue to many gynecologic disorders.

The author stresses the importance of systemic examination including physical examination, blood studies, blood pressure, and urine analysis. Symptoms and lesions pointing to extragenital pathology call for investigation by competent clinicians. The gynecologist who concentrates on the pelvic and vulval areas to the exclusion of the rest of the body may expose himself to serious error and the patient

*Diagnosis in Gynecology (A Classification of Gynecological Diseases Based on Etiology and the Clinical Logic for Diagnosis). By James V. Ricci, A.B., M.D. Philadelphia: The Blakiston Company, 1948. Price \$4.50.

to serious postoperative complications. The author decries the failure of the specialty of gynecology to retain the mammary glands in its own particular therapeutic sphere. A detailed discussion of abdominal examination from the point of view of the gynecologist is presented.

In the chapter on gynecologic examination the author describes in detail the technic of bimanual examination. The traditional use of the left hand is said to have originated in the preantiseptic age of meddlesome gynecologic therapy when the examiner needed his useful hand to handle the diverse instruments then used. The author recommends the use of the right hand and describes methods for overcoming the disadvantages of short fingers and for facilitating palpation of the uterus in obese patients. The speculum examination is placed following the bimanual examination contrary to the practice of many gynecologists who prefer to visualize the cervix and vagina before palpation. Special types of gynecologic examination are listed and discussed but cytologic study for the detection of carcinoma is omitted. A brief outline for examination of sterility patients concludes this chapter.

IN THE following chapter gynecologic symptoms are classified in the order of their frequency. Pelvic pain, vaginal bleeding, and leukorrhea are given as the most common symptoms. The nature of each symptom in relation to the responsible disease is described. Ten major groups of gynecologic diseases are listed and separately discussed in the next chapter which includes a comprehensive breakdown of each group into its component types of disease. For example, under inflammatory disease the pathologic entities produced by the gonococcus, the staphylococcus and streptococcus

and the tubercle bacillus are listed, as are reactions of various parts of the genitals with characteristic tissue response produced by such invaders as the luetic spirochete, the Donovan body, bacillus Ducrey, the bacillus crassus, viruses, worms, protozoa, and fungi.

Psychosexual phenomena while listed as a major gynecologic disease are accorded only a very brief paragraph in which the author states that such entities must be considered borderline conditions which perhaps belong to the clinical realm of the psychiatrist rather than the gynecologist.

The remaining seven chapters of the text are devoted to the classification and discussion of diseases based on etiology according to the involved anatomic portions of the female genital tract. Dermatologic diseases of the vulvovaginal and perineal areas are first discussed followed by a classification and discussion of vulvoperineal diseases, diseases of the vagina, the cervix, uterus, tubes, ovaries, genital ligaments, and parovarium. The discussion of each disease entity includes a description of clinical manifestations, diagnosis, and differential diagnosis.

The method used by the author in organizing the text necessarily leads to a certain amount of repetition. Since, however, the text is intended primarily for instructors and postgraduate students this repetition is of advantage because of its impression value. The general practitioner should find the text valuable particularly as a desk reference for diagnostic problems in this field. The material is well indexed to facilitate such reference. By omitting illustrations and bibliography the author has been able to consolidate a large amount of information into a book of only 259 pages. The text should be considered a definite contribution to gynecologic teaching.

M. B. S.



MEN OF MEDICINE

Fifty Years for the General

SURGERY's spryest veteran, Dr. Willard Bartlett of St. Louis, marked this month (September) his fiftieth year in active practice. But the bald-headed, little abdominal operator with the card-index memory persists in recalling that he might have become a musician.

As a youth in his native Illinois, he was an avid piano student, sang in a regional glee club, played the cornet with a band. "My musical talent, if carried out," he often says wistfully, "might have given the waiting world one more long-haired artist instead of a bald-headed surgeon."

The fact is that Willard Bartlett the musician never had a chance. As the diminutive St. Louisian is fond of noting, there had been surgeons in the family since the Revolutionary War, when Josiah Bartlett maintained a topflight practice which he halted long enough to found the New Hampshire State Medical Society and become the second signer to the Declaration of Independence. Three of Josiah's sons, augmented by a couple of related Bartletts, gave the family six notches in its surgical belt during the revolution. Later, Dr. Willard Bartlett's father, A. T. Bartlett, served as a Union Army surgeon during the Civil War. He lived to be 88—in part, some members of the family suggest lightly, because he wished to see son Willard headed unswervingly on a lifetime given to the practice of surgery.

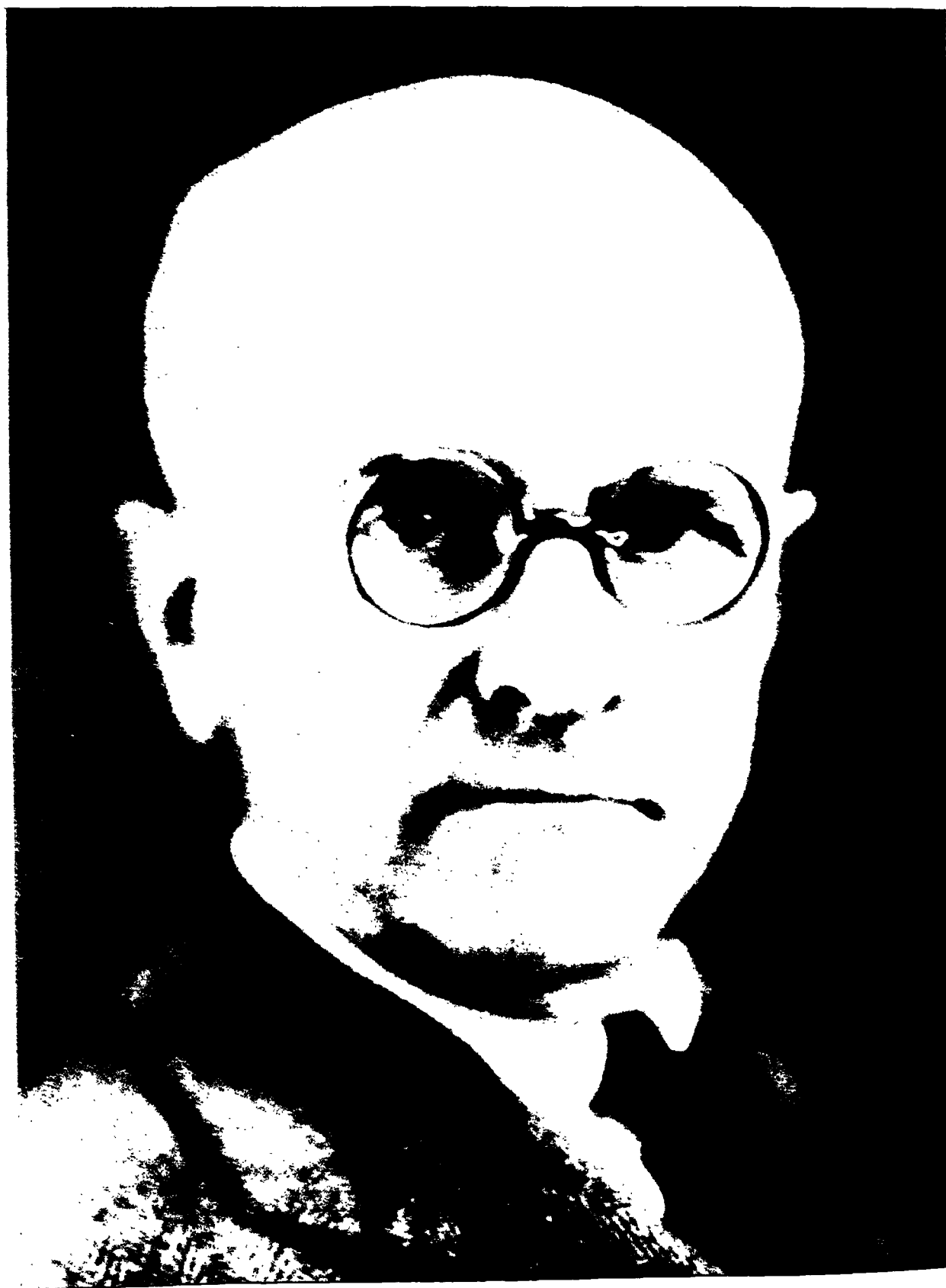
Subsequent developments suggest that if Willard Bartlett were given the proverbial opportunity to do it all over again, he would neatly impale his musical chances on the point of a scalpel and go back to the operating room. For one thing, two of his three sons have followed him in surgery, very obviously to his extreme pride. Moreover, there is scarcely anything which delights him more than the sight of one of his nine grandchildren,

Willard III, playing doctor in juvenile fashion with his grandpa's old stethoscope and instrument bag. But the chief test is that although he has had the opportunity for at least fifteen years now, he persists in refusing to acknowledge the existence of the word "retire." Although he returned, in some degree, to active surgery during the war years, when his sons were in service, it isn't a matter of stubbornness with the elderly surgeon, but a labor of love.

Six days a week, like well-oiled clockwork, he shows up at his midtown St. Louis office. Much of the time he spends as a consultant. Most of the time he devotes to reflective correspondence with those of his old friends who are left, out of the days when individual brilliance, somewhat less than attention to refinements, marked the surgical operator.

In the case of Willard Bartlett, this is a subject of no small moment. Among his cherished comrades today are Dr. George Dock of Pasadena, now 88, Dr. Fred Lund of Boston, and Dr. Rudolph Matas of New Orleans, whom Dr. Bartlett, himself one of the founders of the College of Surgery, firmly regards as the father of vascular surgery. A partial roster of his other comrades in arms, many of them gone, reads like a medical Who's Who. An inveterate traveler, he made many trips to Europe with Harvey Cushing, John Finney, George Crile and Elliott Cutler, when all of these were active members of the Society of Clinical Surgery.

Most warmly of all, he remembers Charlie and Will Mayo. Dr. Bartlett first met the latter when he came to St. Louis to demonstrate an operation on the common bile duct. The St. Louisian, freshly returned from postgraduate studies in Germany, was then only an assistant to the brilliant Dr. A. C. Bernays.



WILLARD BARTLETT

From that encounter over somebody's bile duct came a kinship that was to last a lifetime. Beginning in 1902, Dr. Bartlett made almost annual visits to Rochester. When he developed his original method for drying, sterilizing, and storing catgut in pliable form, it was the Mayos, he recalls, who introduced it into their operating rooms and gave it impetus throughout the profession. The method, which cut drastically into the incidence of postoperative stitch abscesses, resulted from Dr. Bartlett's recognition that previous sterilization methods did not remove from surgical catgut the anthrax which came with it out of sheep's intestines. He literally boiled the gut in oil and stored it effectively in methyl alcohol. The Mayos quickly perceived its value.

When he was past 70, Dr. Bartlett picked up the knack of touch-typewriting, to help him set down in written form his enthusiasm for the life he has lived. In the 200-page memoirs, which he completed just last month, he wrote of "the indefinable human something Dr. Will and dear old Charlie possessed—that truly gracious quality which turned visiting doctors into consultants and every patient into a devoted friend. Many of us sit idly by to see a dream come true. These men of destiny were eager to give all of themselves to *make* one come true."

The quotation serves as a key to Dr. Bartlett himself. It evidences the flare for phrase-making that was exhibited years ago when he was wont to say, in summing up his unyielding disinclination to operate on moribund patients, "Let them do their own dying." It displays, too, a mellowness and a sentimentality that his own sons sometimes failed to perceive in the days when he was setting the pace in the field of toxic goiter surgery. To his boys, he was always "The General." Dr. Willard Bartlett, Jr. confesses ruefully, "We kids were scared to death of him."

His perfectionism, stiffened by his student days among the Germans, made him a tiny terror whose demands upon others for operating room efficiency were exceeded only by the demands he placed upon himself.

During two periods in his career when he was laid low by pleurisy attacks brought on by overwork, Dr. Bartlett formed the practice of coming

home in the afternoon and going immediately to bed, where he had supper and then made notes on the day's work. "Dear me, I did do that, didn't I?" he now says disarmingly, when reminded of it.

LIKE all his memories, Dr. Bartlett's recollections of his childhood in Virden, Illinois, a hamlet near Springfield, are clear and vivid. He recalls watching his father perform operations on kitchen tables. The greatest lesson he believes he took from those days was in being reminded that there is a time when not to operate.

An outstanding boy debater, he took his bachelor degree from Illinois College in Jacksonville, then wrote a thesis on kidney stones to win a master's sheepskin. When he went to St. Louis in 1892 to enroll in the first three-year course offered at what was then Marion Sims, the city had twelve medical colleges. "With but few exceptions," he remembers, "they were either eclectic, homeopathic, or diploma mills."

Still, the young Bartlett felt fortunate. Attending Rush Medical College, his father had been forced to squirm through three years of the same set of lectures repeated three times. The son listened to the same lectures only twice.

It was at his father's suggestion that he went to Germany for further study at Berlin, Strasbourg and Rostock. It was not, he says, until he began to dream in German, that he knew he truly was ready to soak up the technic and atmosphere of German science. Before he completed his German phase, he was to study with some of the great men of the age, teach a course himself in morbid anatomy—in German—and absorb an utter admiration for the best of the German spirit.

In Berlin, one of his first teachers was the pathologist, Rudolph Virchow. On their first meeting, the short-statured American took him for a janitor. "I wish to find Dr. Virchow," he said. The pathologist motioned for him to follow, led the way to the laboratory, took off his coat and said, "Little one, you have found him."

His stay in Germany enabled him to be on hand when Roentgen made his first announcement and gave his first public demonstration of his x-ray discovery from the Crookes vacuum tube. It is to

his Teuton training in chemistry and applied science that Dr. Bartlett attributes the discoveries in which he takes greatest pride.

Until recently, he never had thought to speculate on what achievement in fifty years of practice gave him maximum satisfaction. When asked, he took only a moment to skip coldly by his recognized feats of surgical dexterity, in favor of a piece of research carried on in 1910 with Dr. Joseph Erlanger. In it, the pair demonstrated that shock went with dilation of the blood vessels.

The Bartlett method for sterilizing catgut without losing its pliability came along in 1898. In 1913, tired of operating by light filtering through soot-covered or snow-packed skylights, he developed an operating room lighting system which for the first time employed electric light focused on the field from eight different sources. Reported on in 1913 as the "No-Shade" light, it drew praise from governmental sources, who said Dr. Bartlett had developed "a new principle in optics." The veteran surgeon likes to think that the operating room lighting systems of today are simply refinements of his basic principle. He declined a government basic-patent offer.

In 1910 came the first of his many trips to Europe with Charles Mayo, George Crile, J. B. Murphy of Chicago, and other leaders in the Society of Clinical Surgery. Already, the ambidextrous, deceptively slow-moving Bartlett had won respect for the way in which he achieved speed without haste at the operating table. He was in the vanguard of those who learned to fit operative technic to patient resistance by stages, appeared again in the front ranks when surgery began to shift its emphasis in the direction of preparing a patient before surgery rather than nursing along his strength in the midst of it. "Today," he now observes stiffly, "no operation on toxic goiter will be performed until the patient first is perfectly restored to general health."

Like so many of the surgeons who operated in the period preceding the growth of the residency system, Dr. Bartlett had his own team of operating room assistants and nurses. His favorite assistant, a woman, is with him still, as much in the role of family friend as of nurse.

In 1922, the year he was named vice president of

the American Medical Association, Dr. Bartlett published the first of two eminently successful books. This initial effort was "The After Cure of Surgical Patients," in which he startled many a professional colleague with talk of early postoperative ambulation, a policy he had begun to follow in his own practice twenty years before. In typically brisk and modest fashion, he attributes to his research for the book his special interest in thyroid diseases.

"I wrote the book to learn," he says reflectively.

His other top volume, "Surgical Treatment of Goiter," was issued in 1926. By that time he had struck up a friendship and was maintaining a reciprocally enthusiastic correspondence with Dr. Arthur E. Hertzler of subsequent "Horse and Buggy Doctor" fame. When Hertzler heard quite by accident, in 1926, that Dr. Bartlett was having his goiter volume published, the late great Kansan withheld for a year a pending book of his own on the same subject. Dr. Bartlett treasures a copy of the "Horse and Buggy Doctor," autographed for him in 1946 by Dr. Hertzler. In it, the author wrote on the flyleaf, "To a big little guy who now becomes bigger with the pressure of the years—by one privileged to see and understand the growth."

From several standpoints, Willard Bartlett undoubtedly is one of the most expert husbands in the medical profession. Not that he has kept better than average hours, but it is a rare man indeed who can face a typewriter at the age of 80 and confidently and tenderly peck out a description of the dress his wife wore on their honeymoon decades before. Dr. Bartlett turns this neat and disturbing trick in his memoirs, coupling it with a flowing tribute to the vivacious Genevieve Wilson, markedly his junior, whom he married in St. Louis in 1899.

Falling prey to his direct, engineering mind, he now recalls, he left his bride in a New Orleans courtyard during their honeymoon while he dropped in for a brief visit with his friend, Dr. Matas. He became so absorbed in a Matas operation that he stayed away for several hours, precipitating an early crisis that almost upset the connubial boat.

Mrs. Bartlett soon became accustomed to this, however, friends note, since the couple has enjoyed a close and fruitful kinship. It was not until later, presumably, that the surgeon's wife, herself a woman of diverse interests, heard of the comment her father-in-law made upon meeting her for the first time as a Bartlett-intended.

"Aren't you afraid," the old Civil War physician demanded, assaying the brief frame of his son's fiancée, "Aren't you a little afraid that you'll turn the Bartlett rats into mice?"

His father's fears, Dr. Bartlett hastens to note, proved entirely groundless. One of the couple's sons is a spanking six feet tall, and a second son is very nearly that.

Spurred by his two serious bouts with pleurisy, Dr. Bartlett early developed a studied conservation of his energies and augmented this with a planned program of good, rugged exercise. He never smoked, rarely took a drink, at this late stage of the game sometimes permits himself one old-fashioned to dilate his coronaries.

South of St. Louis, on a 10-acre lot overlooking the Mississippi River, he acquired a log cabin in the twenties to which he promptly dedicated every family weekend. His sons remember their days at the place—which was named "Klein Aber Mein" (Little—But Mine)—with considerably more pungency than their father does.

"It was manual labor every weekend," one of the Bartlett boys has said. "We cleared the 10 acres ourselves with scythes and sickles, and did all our own cooking. The place was on top of a high bluff. We'd climb the bluff, work all weekend, then fall back down the bluff and crawl into the city Sunday night. Father doted on it, and kept going there until clear into his 50's."

The old surgeon remains unconvinced. He believes, now that the river retreat has been sold, that his sons constantly are making up to its present owners in an attempt to angle invitations and receive some of their childhood times.

Perhaps he would not have retained his zest for surgery, nor his present hearty state of health, had he not followed the open road with such insistent regularity. Sometimes as a visiting surgeon for the United Fruit Company, more often on his own, he has made fully 18 trips to Central and South

America, especially Honduras, giving medical lectures at various South American medical schools but keeping his sharp, observant eyes open for local color and custom.

Early in his travels southward, he acquired an interest in reptiles, which he considers much maligned. In 1930, he went so far as to undertake a Central American snake hunt for the St. Louis zoo, in the company of several zoo men, one of them—Marlin Perkins—since become head of the Brookfield Zoo in Chicago. With effervescent delight, he recalls an occasion when a native hooked his only pair of trousers through a porthole on the waterfront of San Salvador. He spins knowing yarns not only of snakes and snarers, but of architecture and music in foreign lands.

HE was a stern character in the operating room, an efficient machine who often singled out difficult cases as a challenge and drove himself unmercifully, he seems to have made up for it with a precocious sense of humor in the conduct of his social relationships.

Bald at an early age, Dr. Bartlett for many years owned a toupee, but intimates insist he wore it only on chilly days, to keep warm, and never for vanity. Dr. Bartlett's days as a wig wag ended when the family dog seized the hairdo one day and chewed it beyond recognition.

Dr. Bartlett took up golf after he was 60. Although his friends observe that he can't play worth a lick, and he admits in candid moments that their appraisal is valid, he went at it with the same overpowering enthusiasm which seems to have marked everything he has tackled. He has continued to be a spectator at many top golf tournaments, always finding a speech to deliver or a meeting to attend in the general vicinity.

When the Professional Golf Association championships were played off in St. Louis last year, Dr. Bartlett was right on hand, wearing an old sun helmet he picked up some years ago in South America and padded faithfully after the golfing greats. He likes to think that Sammy Snead, a family friend, owes his successes since 1940 to a Bartlett pickup. The surgeon ran into Snead in that year and found him in a despondent mood.

Snead said he had been practicing all day before a major tournament, yet his playing was growing worse instead of better.

Dr. Bartlett, quickly assuming a medical stance, prescribed a day on the veranda before a tournament, instead of a day of practice. "Sammy's play improved right off the bat," Dr. Bartlett says primly. "Simple, wasn't it?"

Always a prolific writer—a listing of his medical papers fills several long typewritten pages—the surgeon's output by no means has become completely stalled. Some time ago, a visit to Washington and Lee University in Virginia tickled his interest in the career of Stonewall Jackson. (As a youth, he had bicycled through the Shenandoah Valley.) It was no surprise to friends of the Bartletts when, in one of this year's issues of the *Journal of Surgery, Gynecology and Obstetrics*, there appeared under the Bartlett name a lucid dissertation on the medical care of the wounds that resulted in Jackson's death.

Dr. Bartlett continues these days to engage in a daily hour of calisthenics, a policy he inaugurated about five years ago. Still an avid student of snakes and animals, he rarely misses his daily stroll through the St. Louis zoo. He is scrupulous about maintaining his six-day a week office schedule.

He served during the recent war as a consultant to the Marine Hospital in St. Louis and carried on his sons' practice. That three-way partnership between father and sons, incidentally, ended last year when 47-year-old Willard, Jr., who came out of the Navy a captain, established his own

office. Dr. Bartlett and his second son, Robert, who is 44, continue to share offices. The youngest Bartlett son, A. T. Bartlett, is an executive of the Shell Oil Co. in New York.

A thoroughgoing mystic, Dr. Bartlett recalls that in 1939, after Mrs. Bartlett had left for England to be on hand for the birth of A. T.'s first child, he got the vague feeling that he might not see his wife again. He took a fast boat to England, convinced Mrs. Bartlett after the birth of their grandchild that she should cancel her reservation on a later boat and return instead with him, so he wouldn't be lonely. The ship on which she was to have sailed was the S. S. *Athenia*, sunk halfway through its voyage by a German torpedo.

Dr. Bartlett sits in an office the walls of which are spotted with autographed photos of his great friends, so many of them now dead—Lord Moynehan, Haggard, Mumford, Cushing, the Mayos, Dock, Maras. But he is eminently ready to discuss present-day professional developments, warms to the boon of the antibiotics and the sulfa drugs. Only the advent of operating room air conditioning leaves him, so to speak, cool. This is because, as he explains, "I never was a sweater."

Younger surgeons find him a graphic demonstration of the values of a well-lived life. "The days never seemed dull nor the distances long," he muses. "The recollections of long ago seem as fresh as those of yesterday."

He is titling his memoirs, "One Surgeon Finds The Broad Highway Enchanting." All too few can make that statement.

ROBERT SCHULMAN



EDITORIALS

ETIOLOGY OF RHEUMATISM

THE CAUSE of rheumatic fever like that of rheumatoid arthritis has so far eluded positive identification. A possible bacterial causation, which was the subject of many investigations during the early part of this century, has not been established; it now seems evident that the primary cause must be sought elsewhere.

An editorial in the *British Medical Journal*¹ raises the question as to whether rheumatoid arthritis might be a neurologic disease, and summarizes some of the evidence supporting this hypothesis. The fact remains, however, that the symptomatology and pathology of most cases of both rheumatoid arthritis and of rheumatic fever are more characteristic of an inflammatory disease due to some kind of infection than to a degenerative type of neurologic disorder.

Recently Gordon,² writing on "rheumatism" but discussing principally rheumatic fever rather than rheumatoid arthritis, presents the evidence pointing to a virus causation. One virus, he points out, namely the M₄ virus of Tulloch isolated from pooled smallpox crusts, possesses the power to produce fibrositis in rabbits causing a lesion histologically similar to the predominating lesion in "rheumatism." Another virus, namely that of psittacosis, after passage through mice, exhibits a special capacity to injure the myocardium of the rabbit.

Citing the work which has been done on the agglutination of elementary bodies, Gordon suggests that the evidence obtained from this source consistently points to an interrelationship between rheumatic fever, rheumatoid arthritis, and chorea—a situation which may justify return to the use of the more general term "rheumatism" to include those conditions even when characterized by variety of clinical manifestations. In rheumatic fever, he points out, a suggestively higher proportion of agglutination reactions occurs during the first attack as compared with recurrences. Agglutination also occurred in a striking manner in acute rheumatic fever and acute rheumatoid arthritis, although negative results were obtained in many cases.

The complement fixation test is more delicate than agglutination in detecting specific antibodies to a virus. Such work as has been done with this test is somewhat equivocal. From the evidence available, however, Gordon concludes that the chief infecting agent in rheumatic fever (which is the rheumatic granuloma of Aschoff) is almost certainly a virus.

In the face of failure to identify the causative factors of rheumatic fever and rheumatoid arthritis new possibilities must be investigated and certainly a virus or viruses must be carefully considered. A rickettsial agent is likewise a possibility, particularly since the microscopic pathology of some of the known rickettsial diseases is similar to that of rheumatoid arthritis and rheumatic fever. Similarity of the histologic picture, however, cannot be relied on to prove identity of causation and can be viewed only as a clue and not as evidence. Like-

1. SAVAGE, OSWALD: *Speransky's method of spinal pumping in rheumatoid arthritis*. Brit. M. J. 1:496-497 (March 13) 1948.

2. GORDON, MELVYN: Is rheumatism a virus disease? *Lancet* 354:740 (May 15) 1948.

wise the rabbit as an experimental animal for the investigation of the etiology of rheumatic diseases is of doubtful reliability since this animal³ is particularly obliging in its ability to develop histologic lesions in the heart or joints similar to those found in human beings with rheumatic diseases.

E. P. J.

DOCTORS' DISEASES

ACCORDING to Dublin, Spiegelman, and Leland,* recent death rates for physicians show a lower figure than the general population under age 45 but a slightly higher figure thereafter. Among the ten leading causes of death in physicians, diseases of the heart and blood vessels account for more than half, 54.0 per cent, as would be expected from a similar finding in the general population. But when comparative figures are drawn between specific circulatory disturbances, the mortality figures begin to appear much more significant. Thus the ratio of physicians to white males for "cerebral hemorrhage" is 1 to 20, for "diseases of the heart and coronary arteries" 1 to 18, and for "arteriosclerosis" 1 to 16, a substantial increase in physicians over others. And in the specific instance of coronary artery disease, not only is the physicians' death rate highest in the productive years of 45 to 65, but "compared with the general population, the death rate from these diseases among physicians is the higher by more than 80 per cent."

Granting that much of this excess mortality may be due to better diagnosis, by the same token physicians, who are at least in contact with diagnostic facilities and understand symptoms which might be warnings within their

own selves, should have a lower mortality than the general population, if no other factors were in operation. That such other factors do operate to make this group of circulatory disturbances actually "Doctors' Diseases" seems practically certain.

The studies of Dunbar, Weiss and English, Alexander, Saul, and many others have shown one factor to be almost constantly present in those suffering from coronary heart disease and the essential type of hypertension, *conscious and unconscious emotional tension*. In fact, the characteristic personality type which Dunbar found in the coronary sufferer was: ". . . excessively strenuous work history; the patients worked long hours without vacations under considerable stress and strain. There was regularly a sudden reverse after achieving the goal for which they had been working." Elsewhere she describes the fundamental emotional drive in the coronary patient as an urge to be superior, to rise to the top, to become completely individualistic. This might easily be a description of the average successful physician, and in the light of these observations we can understand why doctors could claim coronary heart disease practically as an occupational hazard.

The point of conflict in the potential coronary victim, Dunbar found, lies in the relationship to authority as first developed with the parents, particularly the father, in the early years of life. A pattern of apparent adjustment to authority, coupled with a deep and lasting unconscious drive to compete with and exceed the father, is then carried over into all activities of life with resultant conflict with all forms of authority, school, business, government, etc., much of which is repressed, building up even more tension. Such a forceful drive to be superior must naturally result in a personality with a strong urge to succeed and considerable likelihood of realizing that ambition. Here again, we might be describing the average successful physician, particularly the type who suffers a coronary attack at a relatively early age.

The most interesting probability about this

3. KEY, J. A.: J. Bone & Joint Surg. 15:67, 1933; JORDAN, E. P.: Arch. Path. 26:274, 1936.

*DUBLIN, L. I., SPIEGELMAN, MORTIMER, and LELAND, R. G.: Longevity and mortality of physicians. Postgrad. Med. 2:188-202 (September) 1947.

concept, however, is the likelihood that the inherent emotional drive probably stimulates the potential coronary victim to seek out a profession, such as medicine. A considerable proportion of doctors come from medical families, which is also in agreement with the well known factors of imitation and environment in psychosomatic disease. Coupled with this head start, it is not surprising that a person with an inherent desire to succeed and be superior, would choose the one profession which

has perhaps a greater characteristic of individualism than any other.

The biblical injunction to "know thyself" deserves consideration by physicians. Psychosomatic studies show unquestionably that recognition of the role of emotional tension in any disease tends to lessen its effect upon the body. We shouldn't wait until 45 to stop and examine ourselves for evidence of tendencies toward the "Doctors' Diseases." By then the damage may already be done.

F. G. S.

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Association Notes

DISTINGUISHED PHYSICIANS FROM OTHER COUNTRIES TO SPEAK AT CLEVELAND

IN ADDITION to the usual outstanding roster of American physicians, the program of the thirty-third Assembly of the Interstate Postgraduate Medical Association at Cleveland, November 9 to 12 inclusive, will also feature several distinguished lecturers from other countries. From Canada will come Dr. Robert M. Janes, Professor of Surgery, and Dr. Ray F. Farquharson, Professor of Medicine, both of the University of Toronto Faculty of Medicine, while London, England will be represented by Mr. Rodney Maingot, F.R.C.S., and Sir Archibald McIndoe, C.B.E., M.S., F.A.C.S., F.R.C.S. Still another leading foreign physician who will address the Assembly is Dr. Tage Kjaer of Copenhagen, Denmark.

Dr. Kjaer, who is affiliated with the Copenhagen Municipal Clinic for Thoracic Surgery, Oresundshospitalet, will speak on the subject, *"Bronchostenosis of Inflammatory, Probably Non-specific Origin."*

Dr. Kjaer was born April 13, 1901, in Copenhagen. He graduated from the Artium in 1926 and received his M.D. degree in 1936. From 1927 to 1932 he served as an assistant at different surgical and gynecological departments in Copenhagen; was assistant at the "Pathologisk Institut" of Copenhagen in 1933; assistant surgeon at the "Københavns Kommune-hospital" from 1934 to 1937; studied surgery in the United States in 1936 and became a specialist in general surgery in 1937. From January 1937 to April 1940, Dr. Kjaer took special training in chest surgery as assistant at the Brompton Hospital, London, England, the Hospital Laennec, Paris, and at the "Sabbatsberg Sjukhus" in Stockholm. From 1941 to 1943 he was chest surgeon at the "Oresundshospitalet" in Copenhagen and in 1944 became chief of chest surgery at that institution.

Dr. Janes graduated from the University of Toronto Medical School in 1916 and shortly there-



MR. RODNEY MAINGOT

after went overseas with the Canadian Army. At the close of the first World War, he returned to Toronto and received the major portion of his surgical training at the Hospital for Sick Children and the Toronto General Hospital, the remainder being obtained at various hospitals in England, particularly St. Bartholomew's. He was appointed to the surgical staff of the Toronto General Hospital and University of Toronto in 1923 and now holds the chair of surgery at the University and is surgeon-in-chief of the hospital. Dr. Janes is a member of the American Association for Thoracic Surgery, fellow of the American Surgical Association, member of the Canadian Society of Clinical Surgeons, fellow of the Royal College of Surgeons of Canada of which he is a member of the Council, and a member of the Central Surgical Association.

Dr. Farquharson, who has been head of the Department of Therapeutics and Professor of Medi-

cine at the University of Toronto Faculty of Medicine since 1934, was born at Claude, Ontario, in 1897. He received the M.B. degree at the University of Toronto in 1922 and served as Junior and Senior Demonstrator in Medicine at that institution from 1928 to 1934. Dr. Farquharson is also assistant attending physician at the Toronto General Hospital, Trustee of the Banting Research Foundation, and a Consultant in Medicine to the Royal Canadian Air Force since 1943. He is a Fellow of the Royal College of Physicians of Canada.

Dr. Farquharson will speak on "*Extreme Insufficiency of the Anterior Lobe of the Pituitary Gland (Simmonds' Disease)*."

British surgeon Mr. Rodney Maingot was born in 1893 and educated in London. Before coming to his present post as Senior Surgeon of Royal Waterloo and South-end General Hospitals, he had been House Surgeon, Chief Assistant Surgical Unit of St. Bartholomew's Hospital, Registrar West London Hospital, Clinical Assistant St. Peter's Hospital for Stone, and Consulting Surgeon, Specialist South-end Victoria Hospital. Mr. Maingot is the author of "The Technique of Splenectomy," published in 1946, "Abdominal Operations," second edition published in 1948, and the recently published "Technique of Gastric Operations." Mr. Maingot's address at Cleveland will be on the "*Surgical Treat-*

ment of Cardiospasm."

Sir Archibald McIndoe will discuss "*Total Reconstruction of the Face in Burns*," when he appears before the Cleveland Assembly. Sir Archibald, who has the degrees of C.B.E., M.B., Ch.B., M.S., M.Sc., F.R.C.S., and F.A.C.S., is Consultant in Plastic Surgery to the Royal Air Force. He was born in Dunedin, New Zealand, in 1900 and received his education at the Otago Boys High School, the Otago Medical School, and the Mayo Clinic. In 1923 he was the St. Bartholomew's Hospital (London) Medallist in Clinical Medicine and Clinical Surgery; Mayo Foundation Fellow from 1924 to 1928; William White Traveling Scholar in 1929; Assistant Surgeon, Mayo Clinic, 1929-30; Chief Assistant to Plastic Department St. Bartholomew's Hospital; Hunterian Professor, 1939.

At present he is Surgeon-in-Charge Queen Victoria Plastic and Jaw Injury Centre, East Grinstead; Plastic Surgeon St. Bartholomew's Hospital; Honorary Plastic Surgeon Chelsea Hospital for Women and St. Andrew's Hospital, and Consulting Plastic Surgeon Royal North Staffs Infirmary, Hospital for Tropical Diseases.

Sir Archibald has been awarded the Commander Order of White Lion (Czechoslovakia); Officer Order Polonia Restituta (Poland), and Commander Order of Orange Nassau (Holland). He is the author of numerous publications on surgical and pathological subjects.

PRESIDENT AND PRESIDENT-ELECT TO SPEAK AT ASSEMBLY DINNER

A PRINCIPAL speaker at the annual dinner of the Interstate Postgraduate Medical Association Thursday evening, November 11, at the Hotel Carter in Cleveland, will be Dr. Herman L. Kretschmer, president of the Association. Dr. Kretschmer is professor of Urology (surgery), at the University of Illinois College of Medicine, Chicago.

Dr. Evarts A. Graham, president-elect of the Association, will also be presented at this function. Dr. Graham is Bixby professor of surgery and head of the department at Washington University School of Medicine in St. Louis.

Heading the Cleveland Committee in charge of meeting arrangements is Dr. David A. Chambers, president, Academy of Medicine of Cleveland and Cuyahoga County Medical Society, and Clinical Instructor in Urology, Western Reserve University School of Medicine. Dr. Chambers is being assisted by a Clinic Committee of which Dr. David Kirk Spittler is chairman and the following are members: Dr. Jac S. Geller, Dr. Carl Hamann, Dr. Robert E. Holmberg, Dr. James I. Kendrick, Dr. Gerald T. Kent, Dr. Fay LeFevre, Dr. W. H. Odell, and Dr. Walter J. Zeiter.

Program

CLEVELAND ASSEMBLY INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

Public Auditorium, Cleveland, Ohio, November 9 to 12, 1948

Tuesday, November 9

8:00 A.M.

8:00 Diagnostic Clinic: "Diet in The Treatment of Hypertensive Disease."

DR. IRVINE H. PAGE, Director of Research, Cleveland Clinic, Cleveland, Ohio.

DR. A. C. CORCORAN, Research Division, Cleveland Clinic, Cleveland, Ohio.

DR. ROBERT D. TAYLOR, Research Division, Cleveland Clinic, Cleveland, Ohio.

8:30 Diagnostic Clinic: "Bronchiectasis."

DR. ROBERT M. JAMES, Professor of Surgery, University of Toronto Faculty of Medicine, Toronto, Ontario, Canada.

9:00 Diagnostic Clinic: "Present Day Rectal Diagnosis."

DR. DOUGLASS PALMER, Assistant Professor of Clinical Medicine, Cornell University Medical College, New York, New York.

9:30 Diagnostic Clinic: "Surgical Complications of Peptic Ulcer."

DR. JOHN D. STEWART, Professor of Surgery, University of Buffalo Medical School; Head of the Department of Surgery, E. J. Meyer Memorial Hospital, Buffalo, New York.

10:00-11:00 *Intermission for Review of Exhibits*

11:00 Diagnostic Clinic: "Lesions of The Colon and Rectum, Dealing Particularly with Malignancies, Polypoid, and Diverticulitis."

DR. RICHARD B. CATTELL, Lahey Clinic, Boston, Massachusetts.

11:30 Diagnostic Clinic: "The Surgical Treatment of Hypertension."

DR. WINCHELL McK. CRAIG, Section on Neurological Surgery, Mayo Clinic; Professor of Neurosurgery, University of Minnesota Graduate School of Medicine, Rochester, Minnesota.

Noon Intermission

1:30 P.M.

1:30 Diagnostic Clinic: "Lesions of The Breast."

DR. ARTHUR PURDY STOUT, Professor of Surgery, Columbia University College of Physicians and Surgeons, New York, New York.

2:00 Diagnostic Clinic: "The Surgical Aspects of Parkinson's Syndrome."

DR. W. JAMES GARDNER, Department of Neurological

Surgery, Cleveland Clinic, Cleveland, Ohio.

2:30 Address: "The Significance of Certain Developments in Electrocardiography in The Analysis of Clinical Problems."

DR. RAYMOND D. PRUITT, Assistant Professor of Medicine, Mayo Foundation, University of Minnesota Graduate School of Medicine, Rochester, Minnesota.

3:00-4:00 *Intermission for Review of Exhibits*

4:00 Address: "The Selection of Cases for The Lempert Fenestra Nov-Ovalis Operation for Restoration of Serviceable Unaided Hearing in Patients with Clinical Otosclerosis."

DR. JULIUS LEMPERT, Lempert Institute of Otology, New York, New York.

4:30 Address: "Trichinosis."

DR. SYLVESTER E. GOULD, Associate Professor of Pathology, Wayne University College of Medicine, Detroit, Michigan.

5:00 Address: "Anesthetic Procedures in The Diagnosis and Treatment of Disease."

DR. CHARLES F. McCUSKEY, Associate Clinical Professor of Surgery (Anesthesia), University of Southern California School of Medicine, Los Angeles, California; President, 1948, The American Society of Anesthesiologists, Inc.

Dinner Intermission

7:30 P.M.

7:30 Address: "The Treatment of Exophthalmic Goiter with Radioiodine."

DR. MAVIS P. KELSEY, Mayo Clinic; Instructor of Medicine, University of Minnesota Graduate School of Medicine, Rochester, Minnesota.

8:00 Address: "Plans for Medical Care of The Veteran."

DR. PAUL B. MAGNUSON, Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, Washington, D. C.

8:30 Address: "Dynamic Therapeutics in Chronic Disease."

DR. HOWARD A. RUSK, Professor of Rehabilitation and Physical Medicine, New York University College of Medicine, New York, New York.

9:00 Address: "Recent Progress in Nutrition."

DR. TOM D. SPIES, Hillman Hospital, Birmingham, Alabama; Professor and Head of the Department of Nutrition and Metabolism, Northwestern University Medical School, Chicago, Ill.

Wednesday, November 10

8:00 A.M.

- 8:00 Diagnostic Clinic: "Use and Abuse of Antipernicious Anemia Substances."

DR. ROBERT W. HEINLE, Associate Professor of Medicine, Western Reserve University School of Medicine, Cleveland, Ohio.

- 8:30 Diagnostic Clinic: "Testicular Dysfunction."

DR. E. PERRY McCULLOUGH, Section of Endocrinology and Metabolism, Cleveland Clinic, Cleveland, Ohio.

- 9:00 Diagnostic Clinic: "Cancer of The Larynx."

DR. CHEVALIER L. JACKSON, Professor of Laryngology and Broncho-Esophagology, Temple University School of Medicine, Philadelphia, Pennsylvania.

- 9:30 Diagnostic Clinic: "The Management of The Elderly Patients."

DR. EDWARD L. BORTZ, Chief, Medical Service "B" in the Lankenau Hospital; Associate Professor of Medicine, University of Pennsylvania Graduate School of Medicine, Philadelphia, Pennsylvania; Immediate Past President, American Medical Association.

- 10:00-11:00 *Intermission for Review of Exhibits*

- 11:00 Diagnostic Clinic: "The Treatment of Bladder Neck Obstruction And Evaluation of Various Methods in Use Today."

DR. HERMAN L. KRETZSCHMER, Professor of Urology (Surgery), University of Illinois College of Medicine, Chicago, Illinois; President, Interstate Postgraduate Medical Association of North America.

- 11:30 Diagnostic Clinic: "Extreme Insufficiency of The Anterior Lobe of The Pituitary Gland (Simmonds' Disease)."

DR. RAY F. FARQUHARSON, Professor of Medicine, University of Toronto Faculty of Medicine, Toronto, Ontario, Canada.

Noon Intermission

1:30 P.M.

- 1:30 Diagnostic Clinic: "The Present Status of Surgical Treatment of Intractable Asthma."

DR. BRIAN B. BLADES, Professor of Surgery, The George Washington University School of Medicine, Washington, D.C.

- 2:00 Diagnostic Clinic: "Surgery of The Colon;—Selection of Cases and Operations of Choice for Malignant Lesions."

DR. CHARLES W. MAYO, Surgical Section, Mayo Clinic; Associate Professor of Surgery, University of Minnesota Graduate School of Medicine, Rochester, Minnesota.

- 2:30 Diagnostic Clinic: "The Use of Prefrontal Lobotomy in The Treatment of Pain."

DR. WALTER FREEMAN, Professor of Neurology, The George Washington University School of Medicine; Consultant and Chief of Service in Neurology, University Hospital; Chief of Service in Neurology, Gallinger Hospital, Washington, D.C.

DR. JAMES W. WATTS, Clinical Professor of Neurosurgery, The George Washington University School of Medicine; Associate in Neurology, University Hos-

pital; Associate in Neurosurgery, Gallinger Hospital, Washington, D.C.

- 3:00-4:00 *Intermission for Review of Exhibits*

- 4:00 Address: "Surgical Treatment of Cardiospasm."

MR. ROBERT MUMFORD, F.R.C.S., London, England.

- 4:30 Address: "Exophthalmos." (The Schneider Foundation Eye Presentation.)

DR. DERRICK VALE, Professor of Ophthalmology, Northwestern University Medical School, Chicago, Illinois.

- 5:00 Address: "Bronchiectasis of Inflammatory, Probably Non-specific Origin."

DR. TIGR KJÆR, Municipal Clinic for Thoracic Surgery, Oresundshospitalet, Copenhagen, Denmark.

Dinner Intermission

7:30 P.M.

- 7:00 "Front Line Surgical Service During The Okinawa Battle." Motion Picture and Narration by

DR. WILLIAM CARMEL ROBERTS, Director, William Carmel Roberts Clinic, Panama City, Florida.

- 7:30 Address: "The Present Status of Cancer Therapy."

DR. R. LEE CLARK, JR., Director and Surgeon-in-Chief, M. D. Anderson Hospital for Cancer Research, University of Texas, Houston, Texas.

- 8:00 Address: "Fluorine in Dental Caries Control."

DR. H. TRENGLEBY DEAN, Dental Director, U.S. Public Health Service; Chief, Dental Research Section Experimental Biology and Medicine Institute, National Institute of Health, Bethesda, Maryland.

- 8:30 Address: "Polypoid Disease of The Colon: What Should We Do About It?"

DR. LOUIS A. BUTE, Mayo Clinic; Professor of Proctology, University of Minnesota Graduate School, Rochester, Minnesota.

- 9:00 Address: "Present Status of The Treatment of Advanced Malignant Disease with Synthetic Estrogens and X-ray Therapy."

DR. FRANK E. ADLER, Associate Professor of Clinical Surgery, Cornell University Medical College; Attending Surgeon and Executive Officer, Medical Board, Memorial Hospital, New York, New York.

Thursday, November 11

8:00 A.M.

- 8:00 Diagnostic Clinic: "The Surgical Aspects of Duodenal Ulcer, Including Complications."

DR. GEORGE G. FINNEY, Assistant Professor of Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland.

- 8:30 Diagnostic Clinic: "Disturbances in The Electrolyte Metabolism of Patients with Nephrosis and Chronic Nephritis in Relationship to Treatment."

DR. IRVING McQUARRIE, Professor of Pediatrics, University of Minnesota Medical School, Minneapolis, Minnesota.

- 9:00 Diagnostic Clinic: "Clinic Illustrating Newer Methods in The Treatment of Hematologic Disorders."

DR. CYRUS C. STRUBBS, Professor of Internal Medicine, Director of Simpson Memorial Institute and Chairman of The Department of Internal Medicine, University of

Michigan Medical School, Ann Arbor, Michigan.

9:30 Diagnostic Clinic: "Gallbladder Disease."

DR. WARREN H. COLE, Associate Dean of the College of Medicine, Professor of Surgery and Head of the Department, University of Illinois College of Medicine; Medical Director and Head of the Operating Room, Research and Educational Hospital, Chicago, Illinois.

10:00-11:00 *Intermission for Review of Exhibits*

11:00 Diagnostic Clinic: "Digestive Diseases."

DR. WALTMAN WALTERS, Mayo Clinic; Professor of Surgery, University of Minnesota Graduate School of Medicine, Rochester, Minnesota.

11:30 Diagnostic Clinic: "Multiple Sclerosis."

DR. HANS H. F. REESE, Professor of Neuropsychiatry, University of Wisconsin Medical School, Madison, Wisconsin.

Noon Intermission

1:30 P.M.

1:30 Diagnostic Clinic: "Diseases of The Spleen."

DR. FRANK H. LAHEY, Director, Lahey Clinic; Surgeon, New England Deaconess and New England Baptist Hospitals, Boston, Massachusetts.

2:00 Diagnostic Clinic: "Surgical Diseases of The Lungs."

DR. EVARTS A. GRAHAM, Bixby Professor of Surgery and Head of the Department, Washington University School of Medicine, St. Louis, Missouri; President-Elect, Interstate Postgraduate Medical Association of North America.

2:30 Diagnostic Clinic: "The Diagnosis and Treatment of Mediastinal Tumors."

DR. ALTON OCHSNER, William Henderson Professor of Surgery, Tulane University of Louisiana School of Medicine, New Orleans, Louisiana; Director of Section on General Surgery, Ochsner Clinic, New Orleans, Louisiana.

3:00-4:00 *Intermission for Review of Exhibits*

4:00 Address: "Total Reconstruction of The Face in Burns."

SIR ARCHIBALD McINDOE, C.B.E., M.S., F.A.C.S., F.R.C.S., London, England; Plastic Surgeon St. Bartholomew's Hospital; Surgeon-in-Charge Queen Victoria Hospital, East Grinstead. Consultant in Plastic Surgery to the Royal Air Force.

4:30 Address: "Version."

DR. CARL HENRY DAVIS, Wilmington, Delaware, Obstetrician and Gynecologist, St. Francis Hospital; Gynecologist, Delaware Hospital; Consulting Obstetrician and Gynecologist, Wilmington General Hospital; Formerly Clinical Professor of Obstetrics and Gynecology, Marquette University School of Medicine, Milwaukee, Wisconsin.

5:00 Address: "The Practical Application of Isoimmunization by the Rh Factor."

DR. PHILIP LEVINE, Director, Biological Division, Ortho Research Foundation, Raritan, N. J.

ASSEMBLY DINNER

The Rainbow Room—Hotel Carter—Informal

7:00 P.M.

For members of the profession, their ladies and friends.

Program

Welcome, and presentation of President Dr. Herman L. Kretschmer, Chicago, Illinois, by

DR. DAVID A. CHAMBERS, President, Academy of Medicine of Cleveland and Cuyahoga County Medical Society, Cleveland, Ohio; General Chairman, 1945 Cleveland Assembly of the Interstate Postgraduate Medical Association of North America.

Addresses

"Medicine and Philately."

DR. HERMAN L. KRETSCHMER, President, Interstate Postgraduate Medical Association of North America; Professor of Urology (Surgery), University of Illinois College of Medicine, Chicago, Illinois.

Presentation of Dr. Evarts A. Graham, President-Elect of the Interstate Postgraduate Medical Association of North America; Bixby Professor of Surgery and Head of the Department, Washington University School of Medicine, St. Louis, Missouri.

"Greetings from England."

SIR ARCHIBALD McINDOE, C.B.E., M.S., F.A.C.S., F.R.C.S., London, England; Plastic Surgeon St. Bartholomew's Hospital; Surgeon-in-Charge Queen Victoria Hospital, East Grinstead. Consultant in Plastic Surgery to the Royal Air Force.

"My Life As A Spy."

By an espionage agent of one of our Allies—a thriller—
(Name withheld)

Friday, November 12

8:00 A.M.

8:00 Diagnostic Clinic: "Management of Renal Lithiasis."

DR. CHARLES C. HIGGINS, Department of Urology, Cleveland Clinic, Cleveland, Ohio.

8:30 Diagnostic Clinic: "Gouty Arthritis."

DR. JOHN H. TALEOT, Professor of Medicine, University of Buffalo School of Medicine, Buffalo, New York.

9:00 Diagnostic Clinic: "Important Points in The Differential Diagnosis Between Malignant and Benign Breast Lesions."

DR. CHARLES F. GESCHICKTER, Professor of Pathology, Georgetown University School of Medicine, Washington, D.C.

9:30 Diagnostic Clinic: "Cancer of the Urinary Bladder."

DR. GILBERT J. THOMAS, Associate Clinical Professor of Surgery (Urology), University of Southern California School of Medicine, Beverly Hills, California.

10:00-11:00 *Intermission for Review of Exhibits*

11:00 Diagnostic Clinic: "Diagnosis and Treatment of Cirrhosis of The Liver."

DR. W. PHILIP COZZ, Associate Professor of Medicine, College of Medical Evangelists, School of Medicine, Riverside, California.

11:30 Diagnostic Clinic: "Painful Conditions of The Foot and Ankle."

DR. PHILIP LEWIN, Professor of Bone and Joint Surgery, Northwestern University Medical School, Chicago, Illinois.

Noon Intermission

1:00 P.M.

1:00 Diagnostic Clinic: "Radio-active Iodine for The Treatment of Thyroid Disease."

DR. GEORGE CAILE, JR., Cleveland Clinic, Cleveland, Ohio.

1:30 Address: "Diagnosis and Surgical Treatment of Intrathoracic Extrapulmonary Tumors."

DR. STUART W. HARRINGTON, Mayo Clinic; Professor of Surgery, University of Minnesota Graduate School, Rochester, Minnesota.

2:00 Address: "The Clinical Management of Diarrheas."

DR. CHAUNCEY D. LEAKE, Vice-President, The University of Texas—Medical Branch; Professor of Pharmacology, University of Texas School of Medicine, Galveston, Texas.

2:30-3:00 Intermission for Review of Exhibits

Dismantling of the exhibits will begin at 3:00 P.M.

3:00 Address: "Prophylaxis and Treatment of Eclampsia."

DR. WILLIAM F. MENGERT, Professor of Obstetrics and Gynecology and Chairman of the Department, Southwestern Medical College of Southwestern Medical Foundation, Dallas, Texas.

3:30 Address: "Surgical Treatment of Polyps of The Colon."

DR. FRED W. RANKIN, Lexington, Kentucky, Clinical Professor of Surgery, University of Louisville School of Medicine, Louisville, Kentucky.

4:00 Address: "The Emergency Treatment of Apoplexy."

DR. GEZA DE TAKATS, Associate Professor of Surgery, University of Illinois College of Medicine, Chicago, Illinois.

4:30 Diagnostic Clinic: "Surgery of the Heart with Special Reference to Coronary Artery Disease."

DR. CLAUDE S. BECK, Professor of Neurosurgery, Western Reserve University School of Medicine, Cleveland, Ohio.

PLACE OF ASSEMBLY

The members of the Assembly will have the pleasure of convening in the Cleveland Public Auditorium. Its equipment is modern in every detail and meets every requirement to carry on the Assembly successfully, such as acoustics, seating capacity, large stage, temporary hospital, electrical equipment, etc.

The opening session of the scientific and clinical program will begin promptly at 8:00 o'clock Tuesday morning, November 9, 1948.

Registration

The registration fee for the four-day session is \$5.00.

Doctors in uniform, Internes, Graduate Nurses, Technicians and Dietitians will be admitted upon the payment of \$1.00 registration fee. Senior medical students and senior student nurses will be admitted free of charge Friday, November 12, only, and upon presentation of proper credentials at the registration desk.

Guests of the Association (i.e., those appearing on the scientific and clinical program) are requested to register.

Life Members are requested to show their Life Membership cards at the time of registration.

Cleveland physicians are urged to register in advance of the opening of the Assembly, Monday afternoon, November 8, at the Hotel Cleveland.

Place of Registration

The main Registration Department will be at the Cleveland Public Auditorium. This department will open Tuesday morning, November 9.

Everyone attending the Assembly must register. A distinctive badge will be issued to all professional men and women at the time of registration, and a distinctive button will be issued to the senior medical students and senior student nurses. No one will be permitted to attend the scientific and clinical sessions or visit the exhibits unless a badge or button is shown. It is suggested that the badge or button be worn. Your cooperation in this matter is requested.

Technical Exhibits

CLEVELAND ASSEMBLY INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

ABBOTT LABORATORIES North Chicago, Ill. Booths 133-134

You are cordially invited to inspect the entirely new exhibit prepared for this meeting. We are confident it will excite your attention and interest. Abbott Professional Service Representatives in attendance will welcome an opportunity to discuss the newer medical developments with you. Make a visit to the Abbott booth a MUST in your technical exhibit itinerary.

THE ALKALOL COMPANY Taunton, Mass. Booth 22

ALKALOL, an alkaline, nontoxic, bland solution for the treatment of the mucous membranes of the eyes, nose and throat; and as an effective wet dressing in many indications. Alkalol is an excellent vehicle for penicillin or sulfathiazole. IRRIGOL, a powder which in solution makes an aseptic, slightly astringent vaginal douche. It is also widely used for colonic irrigations and rectal enemas. ALKALOL and IRRIGOL ethically promoted since 1896.

W. D. ALLISON COMPANY Indianapolis, Ind. Booths 111-112

Two completely new developments in medical furniture will be displayed for the first time at this year's I.P.M.A. meeting. These new products are a complete suite of examination room furniture, and a consultation room desk. Their modern professional design gives them a clear-cut beauty that is different! They merit your consideration, and we look forward to seeing you in Cleveland.

A. S. ALOE COMPANY St. Louis, Mo. Booths 105-106-107

The representatives of the A. S. Aloe Company will welcome their friends at their booths, where they will have on display a representative cross section of our complete line of Surgical, Hospital, and Laboratory equipment and supplies. Featured will be a complete line of government surplus instruments available at the present time—especially selected, fully certified instruments at approximately one half the regular cost.

AMERICAN HOSPITAL SUPPLY CORPORATION Evanston, Ill. Booth 101

The American Hospital Supply Corporation will exhibit the following: the full range of Baxter Parenteral Products—Intravenous Solutions, including the new Protein Hydrolysate Baxter, Blood Transfusion and plasma equipment plus disposable accessories for the administration thereof; Blood grouping Serums that excel in accuracy, speed and dependability. The new Tomac Oxygen-Nebulizer for inhalation therapy that effects a 50 per cent saving in gas and drugs; and certain selected Tomac products that simplify, if not solve many hospital problems.

AMERICAN OPTICAL COMPANY Buffalo, N. Y. Booth 218

The Scientific Instrument Division of the American Optical Company will exhibit the new Spencer Phase Microscope, with a selection of objectives in dark, medium, and B-minus contrast. In addition, the pocket-sized Hb-Meter, which allows rapid hemoglobin determinations to be made at the bedside, will be on display, as well as the Bright-Line Haemacytometer, and several standard microscopes of Spencer quality.

AMES COMPANY, INC. Elkhart, Ind. Booth 220

Ames Company representatives will be glad to discuss Decholin, the standard hydrocholeretic agent for the treatment of biliary tract diseases, and Decholin Sodium, pure sodium dehydrocholate. They will be demonstrating Clinitest and Hematest—simplified tests for the detection of urine sugar and occult blood.

APPLETON-CENTURY-CROFTS, INC. New York, N. Y. Booth 126

Such new 1948 titles as Maingot's *Abdominal Operations*; Morrison's *Ear, Nose and Throat*; Cole and Elman's *General Surgery*; Burstein and Bloom's *Electrocardiography Atlas*; Zinsser's *Bacteriology* (under new authorship); and Thomson and Negus' *Nose and Throat* will be featured in the Appleton-Century-Crofts exhibit in Booth 126. Also on display are the latest editions of Osler's *Medicine* and Kolmer's popular monograph on *Antibiotic Therapy* together with other standard titles regularly advertised in POSTGRADUATE MEDICINE.

ARMOUR LABORATORIES Chicago, Ill. Booths 35-36

The Armour Laboratories, a pioneer in the field of Endocrinology, will welcome members of the Interstate Postgraduate Medical Association to visit the Armour exhibit in Booths 35 and 36. If you have not received copies of Armour booklets on "THE THYROID GLAND," "Function and Malfunction of the Biliary System," and the "Armour ATLAS of Hematology," you may secure them at the Armour booths.

THE GORDON ARMSTRONG COMPANY, INC. Cleveland, O. Booth 56

The Armstrong X-4 Baby Incubator, which will be on exhibit at the I.P.M.A. Meeting, is designed to furnish safe heat, humidity and oxygen for any newborn baby. They are used not only for premature babies, but for any underweight or debilitated baby that may need special treatment. The Armstrong X-4 Baby Incubator is the only Baby Incubator ever tested and approved for use with oxygen by Underwriters' Laboratories. It also carries the Seal of Ac-

ceptance of the American Medical Association, and the Approval Seal of the Canadian Standards Association. That the Incubator is both effective and practical is evidenced by the fact that over 5,000 of them are now in use all over the world.

AYERST, McKENNA & HARRISON
New York, N. Y.
Booth 164

"Premarin" (Estrogenic Substances—water soluble), a highly effective and well tolerated preparation of naturally-occurring, orally-active, conjugated estrogens (equine). The potency of "Premarin" is expressed in terms of its principal estrogen, sodium estrone sulfate. "Premarin" is available in tablets of four potencies and also in liquid form.

THE BABEE-TENDA CORPORATION
Cleveland, O.
Booth 222

THE BAKER LABORATORIES, INC.
Cleveland, O.
Booth 192

The Baker display is built around the six-step approach to optimum infant nutrition. An adjusted protein, two carbohydrates, a modified fat, vitamins, soluble mineral salts and iron, coupled with simplicity of preparation and low cost, provide for complete nutrition and insure cooperation in the home. Baker's Modified Milk, liquid or powder, may be used interchangeably from birth to the end of the bottle-feeding period. May we discuss your infant feeding problem with you?

BARD-PARKER COMPANY, INC.
Danbury, Conn.
Booth 82

Genuine Bard-Parker "Rib-Back" surgical knife blades—"the blade that assures cutting efficiency"; surgical knife handles, including long handles for deep surgery, hysterectomy and eye handles and laboratory handles; Bard-Parker Formaldehyde Germicide—a sporicidal solution; instrument sterilizing container; Chlorophenyl, an ideal office and ward instrument disinfectant, Hematologic cases for obtaining bedside blood samples, and pipettes.

A. C. BARNES COMPANY
New Brunswick, N. J.
Booth 213

The A. C. Barnes Company cordially invites all physicians to visit their new exhibit, ARGYPULVIS, a recent addition to the BARNES line, will be featured by a series of illuminated color transparencies depicting an effective new treatment for Trichomonas vaginalis vaginitis. Literature and professional samples will be available, ARGYROL and OVOFERIN also will be on display. See the BARNES color and sound films—"Cervicitis—Etiology and Treatment," and "Non-Operative Treatment of Paranasal Sinusitis," at the Scientific Motion Picture Exhibit.

BARRY LABORATORIES, INC.
Detroit, Mich.
Booth 161

The Barry Laboratories will display for the consideration of their many physician friends new and modern diagnostic allergy skin testing sets. There will be assortments for all specialties including a special assortment for the general practitioner. The Biological Division of the Barry Labora-

tories will present a complete line of sterile injectables in multiple dose and ampule vials including a high potency, ready mixed B-Complex solution with a long term potency guarantee. The technical representative of the Barry Laboratories will be on hand to assist all physicians inquiring about their products and services.

BAUER & BLACK
DIVISION OF THE KENDALL COMPANY
Chicago, Ill.
Booth 34

Bauer & Black cordially invites you to inspect famous CURITY line of products for doctors, surgeons and hospitals, including new products—Curity Surgical Felt, the *only* true surgical cotton felt, and Kerlix. In addition, there will be shown the Curity suture line, Curity Wet-Proof and regular adhesive tape, the Osteo Plaster line, Curity surgical dressings, Tensor Elastic Bandage, Castex, and the rest of a famous line of products. Visit Booth 34.

W. A. BAUM CO., INC.
New York, N. Y.
Booths 71-72

All models of the Lifetime Baumanometer will be displayed and demonstrated for the doctors in attendance. Those who maintain a central examining place will be especially interested in examining the WALL Model Baumanometer. In addition, a full line of accessories—including special infant and child size bloodpressure cuffs—will be available at the Baum booth.

BAYBANK PHARMACEUTICALS, INC.
New York, N. Y.
Booth 117

You are cordially invited to visit our exhibit for up-to-the-minute information on "Vaseline" Sterile Petrolatum Gauze Dressings, for topical treatment of burns and wounds and for many uses in surgery; NARAKON Nasal Solution Plain or Compound, indicated in upper respiratory affections; LORAKON Collutory, the distinctive ethical and highly efficient gargle and mouth wash; and TERAKON Paste and Ointment Base, the unique universal dermatologic vehicle and improvement over Lassar's Paste.

BECTON, DICKINSON & CO.
Rutherford, N. J.
Booths 66-67

BILHUBER-KNOLL CORPORATION
Orange, N. J.
Booth 115

For information on the latest developments of the medicinal chemicals of Bilhuber-Knoll Corporation, visit our booth. Your discussions will be welcomed on Oenethyl, their new vasopressor; Octin, antispasmodic; Metrazol, analeptic and antianoxicant; Theocalcin, diuretic and myocardial stimulant, and Dilaudid, analgesic and cough sedative. These and their other dependable prescription chemicals are prescribed alone or in combinations with other drugs as the individual patient may require.

THE BIRTCHER CORPORATION
Los Angeles, Calif.
Booth 202

Special attention will be focused on new items at The Birtcher Corporation Booth. The new Blendome "Truly Portable" Electro-Surgical Unit, light weight with big unit

performance, invites your inspection. See the new Improved Hyfrecator, restyled and redesigned by Walter Dorwin Teague, internationally famous industrial designer. Examine the Crystal Bandmaster S. W. Diathermy bearing F.C.C. Type Approval. Don't fail to investigate the Birtcher Electro-Surgical Unit, outstanding for transurethral prostatectomy and general surgery. A cordial invitation extended to all.

THE BLAKISTON COMPANY
Philadelphia, Pa.
Booth 141

THE BLAKISTON COMPANY will have an attractive exhibit of new and standard books. All visitors are cordially invited. In addition, there will be advance information on forthcoming titles of importance to the profession. Ask to see Ricci—*Diagnosis in Gynaecology*; Smith and Gault—*Essentials of Pathology*; Stitt, Clough and Branham—*Practical Bacteriology*; Lillie—*Histopathologic Technic*; Epstein—*Strabismus*; Fuchs—*Diseases of the Fundus Oculi*; Fishbein—*Medical Writing*, and many others.

BORCHERDT MALT EXTRACT COMPANY
Chicago, Ill.
Booth 162

New advances in nutritional supplements for pediatric practice will be featured by Borchardt Malt Extract Company. These include: Malt Soup Extract, now in two forms, Liquid and Powder, for constipation in bottle fed infants; Livipeptone, a high liver, high iron, and high vitamin B-Complex mixture in palatable form for both bottle fed infants and older children; and Thiamalt-Cumaltron mixture, providing a potent copper-iron hematinic and vitamin B-Complex combination, for undernourished children.

THE BORDEN COMPANY
New York, N. Y.
Booth 21

Meet BIOLAC, a liquid modified milk for infant feeding; DRYCO with its formula flexibility; MULL-SOY for your milk allergic patients; powdered whole milk KLIM; the improved milk sugar, BETA LACTOSE; and the MERRELL-SOULE PROTEIN and LACTIC ACID MILKS. We invite your attention to GERILAC, a vitamin-fortified powdered milk for well-rounded nutrition in convalescence, pre- and postoperative diets, geriatrics, pregnancy and lactation, and soft and liquid diets.

BREWER & COMPANY, INC.
Worcester, Mass.
Booths 80-81

This exhibit consists of specialties centering around Theosodate, the original enteric-coated tablet of Theobromine Sodium Acetate, and Luasmin, a combination of theophylline sodium acetate, phenobarbital, and ephedrine for the treatment of asthma. Also, Brewer capsules and ampules, other specialties including Soduxin (Sodium Succinate—Brewer) and standard pharmaceuticals manufactured by Brewer and Company, Inc., including a complete line of vitamin preparations for internal use and injection. Gel-ets, the newest mode in oral vitamin therapy and Amchlor, enteric coated one-gram tablets of ammonium chloride are also featured.

BRISTOL LABORATORIES, INC.
New York, N. Y.
Booths 108-109

Bristol Laboratories, Inc.'s exhibit will be devoted to the

display of many of its antibiotic and pharmaceutical products. Featured will be FLO-CILLIN "96" available in a 10 cc. vial, a 1 cc. cartridge and a Disposable Syringe Package; VYTINIC, a highly palatable liquid hematinic with folic acid; PALAPENT, a palatable elixir of pentobarbital sodium, U.S.P., an excellent prescription vehicle; ALMINATE TABLETS, Bristol's brand of aluminum dihydroxy aminoacetate for the management of peptic ulcer, gastritis and hyperacidity and BARBONATE TABLETS, a companion product containing Alminate with the combination of phenobarbital and belladonna alkaloids to give it an antispasmodic and sedative action. Qualified representatives will be on hand to answer questions and to assist the medical profession.

BRISTOL-MYERS COMPANY
New York, N. Y.
Booth 2

BRISTOL-MYERS COMPANY cordially invites you to visit its booth where BRISTOL-MYERS' representatives will be in attendance to extend a hearty welcome to all visitors and to answer any questions pertaining to SAL HEPATICA and other famous products on display.

BROOKS APPLIANCE COMPANY
Chicago, Ill.
Booth 217

The Brooks Appliance Company will exhibit the following merchandise: Trusses, Bandages, Proctologic Instruments, Elastic Hosiery, and Syringes and Needles. Mr. W. C. Ayer will have charge of the exhibit and will describe in detail the technic of applying the combination pressure bandages, Contura plus Pressoplast, which are used in treating Osteo-Arthritis of the Knee Joints, Phlebitis and Leg Ulcers.

THE BURDICK CORPORATION
Milton, Wis.
Booth 144

The Burdick Corporation will exhibit their complete line of Physical Therapy Equipment. A feature of special interest will be the X 85 Diathermy Unit which has the acceptance of the Council of Physical Medicine, Underwriters Laboratories and the Federal Communications Commission.

BURROUGHS WELLCOME & CO. (U.S.A.), INC.
New York, N. Y.
Booths 131-132

Large THREE-DIMENSIONAL color photography will be used to illustrate the important features of "Wellcome" GLOBIN INSULIN. Be sure to stop by at our booths to see this unusual development.

CAMBRIDGE INSTRUMENT COMPANY, INC.
New York, N. Y.
Booth 156

Cambridge Instrument Company, Inc., will exhibit its line of diagnostic instruments. Among those shown will be the Cambridge "Simpli-Trol" light-weight, portable Electrocardiograph and Electrocardiograph-Stethograph with pulse recorder, the new Cambridge Electrokymograph for recording heart border motion, and the Cambridge Plethysmograph, a new calibrated instrument which makes quantitative and reproducible records. Also on display will be the Cambridge "All Electric" Mobile Electrocardiograph-Stethograph with pulse recorder for hospital and institutional use.

TECHNICAL EXHIBITS

**CAMEL CIGARETTES
MEDICAL RELATIONS DIVISION**
New York, N.Y.
Booths 61-62

Camel Cigarettes will present a dramatic full color review of their recent medical research on smoking, as well as the details of the nationwide survey showing that "More Doctors Smoke Camels Than Any Other Cigarette." Another panel will illustrate the absorption of nicotine in the respiratory tract. Representatives will be present.

CAMERON HEARTOMETER COMPANY
Chicago, Ill.
Booth 207

See the improved Heartometer, a scientific precision instrument for accurately recording systolic and diastolic blood pressures, also furnishing a permanent graphic record of the pulse rate, disturbances of the rhythm, myocardial response, the action of the valves, as well as peripheral vascular circulation. The Heartometer clearly reveals heart disturbances in both early and advanced stages, and is of great value in checking the progress of medication and treatment.

CAMERON SURGICAL SPECIALTY COMPANY
Chicago, Ill.
Booth 11

Have a demonstration of the Cameron Cauterodines and Cauteradiors for Electro-surgery, Electro-cauterization and Electro-coagulation: Coagular-Sigmoidoscope; Electro-Diagnostic Lamps and Instrument Sets; Radiolucent Canula; the new Flexible Gastrosopes with treated and coated lenses; Flexible Esophagoscopes; Bronchoscopes-Endoscopes-Laryngoscopes; Mirror Headlites; Binocular Spectacle Loupe; Magniscope and other Specialties.

S. H. CAMP AND COMPANY
Jackson, Mich.
Booth 160

A series of illuminated transparencies depicting anatomical conditions before and after application of Camp scientific supports will be displayed. Experts in attendance will answer questions pertaining to the scientific application of anatomical supports and advise regarding their availability in the Authorized Service departments of stores throughout the country.

CANADIAN RADIUM & URANIUM CORP.
New York, N.Y.
Booth 103

American-mined and American-refined radium now available to the medical profession in any form and any type of container. Old radium exchanged for new. A complete line of radium instruments, accessories, and protective equipment. See our new-type radium D applicator for treatment of ophthalmic conditions—a revolutionary advance in radiation therapy. For details, visit our booth.

CARNATION COMPANY
Los Angeles, Calif.
Booths 148-149

You are invited to visit Booths 148 and 149 where you will see an attractive display on Carnation Evaporated Milk—"the milk every doctor knows." Some valuable information on the use of this milk for infant feeding, child feeding, and general diet will be presented and the method

by which Carnation is generously fortified with pure crystalline Vitamin D—400 U.S.P. units per reconstituted quart—will be explained. Interesting literature will also be available for distribution.

G. W. CARNICK COMPANY
Newark, N.J.
Booth 6

Professional representatives will welcome the opportunity of discussing with I.P.M.A. members newly-introduced GWC ethical preparations including Thelestrin in Aqueous Suspension, Lutestrogen in Sesame Oil, Neohemochromin Capsules, Dicalossa Tablets, Hemochromin with B-Complex and Vitamin C. Descriptive literature and complimentary supplies of numerous GWC products, including Enterosols Hormotone "T," are available on request.

THE CENTRAL PHARMACEUTICAL COMPANY
Seymour, Ind.
Booth 199

The Central Pharmaceutical display will feature the Synophylate line. Synophylate or Theophylline Sodium Glycinate represents a new and greatly improved theophylline compound for the treatment of asthmatic and cardiac conditions. These products bear the seal of acceptance of the American Medical Association. Entabs and Syrup Neocylate will also be displayed. These products also represent advancements in an important field of therapy; namely, rheumatic fever and allied conditions. Other products for modern therapy will also be shown.

CIBA PHARMACEUTICAL PRODUCTS, INC.
Summit, N.J.
Booths 12-13

Ciba Pharmaceutical Products, Inc. invites you to visit their exhibit for latest information about PYRIBENZAMINE, the antihistaminic for relieving symptoms of allergy. Also displayed will be PRIVINE Hydrochloride, an effective, long-lasting nasal vasoconstrictor, and METADREN LINGUETS, the most potent orally active androgenic hormone in a form suitable for sublingual absorption. Representatives in attendance will be very glad to answer any questions you may have concerning these and other Ciba products.

WARREN E. COLLINS, INC.
Boston, Mass.
Booth 136

WARREN E. COLLINS, INCORPORATED cordially invites you to visit a showing of fine scientific respiration apparatus. These include the Drinker-Collins Duplex Respirator with the latest Minnesota Sloping Front; the Benedict-Roth metabolism apparatus for routine metabolism work and lung function studies; the Collins Open-Top Oxygen Tent and the first showing at the Assembly of the I.P.M.A. of the new waterless Collins Metabolox. The Metabolox has the seal of approval of the Council on Physical Medicine of the A.M.A. Skilled technicians will be in attendance to welcome you.

CREAM OF WHEAT CORPORATION
Minneapolis, Minn.
Booth 110

The Cream of Wheat Corporation cordially invites you to visit their booth to obtain first hand information of both Enriched 5 Minute CREAM OF WHEAT and Regular CREAM OF WHEAT, also ZINC Wheat Germ. You will find

interesting educational material, quantities of which may be obtained by registering. Edward R. Shopp, Director of their Health Education Department, will be in charge.

DAVIES, ROSE & COMPANY, LTD.

Boston, Mass.
Booth 169

It is a pleasure to again be invited to participate in the Annual Assembly of the I.P.M.A. Our representatives, Messrs. H. V. Orne and W. E. Purinton, will be in attendance to welcome you and to explain the merits of the products exhibited, particularly our Pills Stramonium, 0.15 gm. (approx. $2\frac{1}{2}$ gr.), now extensively employed in the sequelae of epidemic encephalitis.

F. A. DAVIS COMPANY

Philadelphia, Pa.
Booth 135

NEW MEDICAL BOOKS—visit Booth 135. *Segmental Neuralgia*—Judovich; *Arthritis*—Bach; *Gallbladder Diseases*—Behrend; *Pre- and Postoperative Care*—Tourish; *General Medicine*—Reimann; *Treatment*—Gruber; *Peripheral Vascular Diseases*—Kramer; *Pediatric Progress*—Litchfield and Dembo; *Medical Diagnosis*—Loewenberg; *Urology*—McCrea; *Dermatology*—Greenbaum; *Cystoscopy*—McCrea; *Diseases of the Chest*—Judd; *Rhinoplasty*—Maliniac; *Gonioscopy*—Troncoso; *Reparative Surgery*—May; *Radiology*—Pillmore; *Diagnostic Signs*—Robertson, and *Cardiovascular Disease*—Stroud.

DAVIS & GECK, INC.

Brooklyn, N. Y.
Booths 208-209

Davis & Geck, Inc., manufacturers of sterile surgical sutures, will present an armamentaria of suture-needle combinations specifically prepared for every type of surgery. Literature on sutures and wound healing will be available. This will include reprints and monographs as well as leaflets dealing with the specific products. Subjects selected from the D & G Surgical Film Library will be presented in the D & G Cinema Room. Programs and catalogs explaining this service may be obtained at the booth.

THE DENVER CHEMICAL MFG. CO., INC.

New York, N. Y.
Booth 225

Galatest for the instantaneous determination of urine sugar, and Acetone Test (Denco) for the detection of acetone in urine will be exhibited. You are cordially invited to visit our booth for demonstration of these "spot tests" for sugar and acetone. Galatest and Acetone Test (Denco) offer advantages of accuracy, simplicity and economy in routine urinalysis.

DePUY MANUFACTURING COMPANY

Warsaw, Ind.
Booths 73-74

DePuy will have on display, for your consideration, Modern Fracture Appliances. The new improved Lorenzo Lag Screw for Subtrochanteric fractures. Also Blount Plates, Moore Plates, and the improved Blade Plate Driver and Extractor. Another thing of great interest to the profession will be the new Jasper Surgical Steinman pin cutter. Mr. V. C. Moss and J. E. Hart will answer any of your questions.

DEVEREUX SCHOOLS

Devon, Pa.
Booth 84

Devereux Schools provide the physician with facilities for the education and treatment of children having academic or emotional difficulties. Twelve Devereux Schools in Pennsylvania and California offer a controlled environment and modern training shaped to the needs of each child. A psychiatrist, two physicians, and a psychologist, all in residence, cooperate with the referring physician in his plans for the child's training and care. Representatives will gladly answer questions or discuss how Devereux may serve you and your patients. John M. Barclay in charge.

THE DeVILBISS COMPANY

Toledo, O.
Booths 49-50

Kodachrome transparencies depicting the distribution of aerosols in the lungs and bronchi are features of The DeVilbiss Company exhibit. This data supports clinical findings and experimental work with aerosols of penicillin, streptomycin, epinephrine and other substances. Other features are x-rays and transparencies that indicate the superior coverage and penetration derived by atomization in the nasal and sinus areas. Instruments for all types of spray application will be displayed.

THE DIETENE COMPANY

Minneapolis, Minn.
Booth 27

Visit The Dietene Company exhibit and discover that really palatable high protein diet supplement—MERITENE. Smell it—taste it—and be convinced. Also see the personal type diet service that is available, without charge, to physicians. DIETENE Reducing Supplement and the 1,000 calorie Dietene Reducing Diet will also be on display. Both MERITENE and DIETENE are Council-Accepted.

DOAK COMPANY, INC.

Cleveland, O.
Booth 175

Colloids of bismuth, calcium, iodine and iron for par-enteral administration in the treatment of arthritis, syphilis, calcium and iodine deficiency. Dermatological preparations for treatment of various skin manifestations.

DOHO CHEMICAL CORPORATION

New York, N. Y.
Booth 14

The makers of AURALGAN are featuring at this meeting their new sulfa preparation o-ros-mo-san, indicated in the treatment and control of chronic suppurative ears. Also, Mallon, Division of Doho, is introducing our new topical anesthesia, RECTALGAN for relief of pain and itching in hemorrhoids and pruritis. Our representatives will be happy to explain in detail the workings of these medications. Also, to distribute hospital aural instruction charts and other charts of anatomic and pathologic diseases of the ear.

DUREX PRODUCTS, INCORPORATED

New York, N. Y.
Booth 198

Contraceptive specialties by Durex will be more than worthwhile investigating. The Bow-Bend Diaphragm (hinged rim) will be of particular interest. Complete contraceptive sets contained in the new compact and sanitary Duracase will be appreciated by the physician and patient.

TECHNICAL EXHIBITS

alike. The latest clinical information on both Lactikol Jelly and Lactikol Creme will be available.

E & J MANUFACTURING CO.

Glendale, Calif.
Booth 190

New E & J developments in respiratory equipment will be displayed by the E & J Manufacturing Company, as well as various models of the E & J Resuscitator-Inhalator-Aspirator. The exhibit will feature the E & J Bassinet Model Resuscitator-Inhalator-Aspirator which provides for adjustable heating, and the E & J Pressure Nebulizer. Resuscitation of infants will be dramatized by the use of E & J equipment on a plastic doll in which the functioning of the lungs can be observed.

J. H. EMERSON COMPANY

Cambridge, Mass.
Booth 122

The Lung Immobilizer for healing tuberculous cavities by complete arrest of lung movement will be shown in J. H. Emerson Company's display. The Dome Respirator, the Emerson Hot Pack Apparatus, and the latest Emerson Resuscitators will also be demonstrated.

ETHICON SUTURE LABORATORIES

New Brunswick, N.J.
Booths 20-119

Two new Ethicon products—Sterile Pack Sutures and Tantalum Gauze—will be featured at the Ethicon exhibit. Sterile Pack is the new disposable metal suture storage canister containing tubed sutures, packaged sterile. Since its release, Sterile Pack has proved conclusively to hospitals all over the country, that it saves personnel, time and dollars in suture handling; and assures suture sterility. Just released, Tantalum Gauze is a 50 x 50 inch mesh made of .003 inch diameter wire which has been used with great success in the repair of large and recurrent hernias, particularly those characterized by tissue deficiencies.

FELLOWS MEDICAL MANUFACTURING CO., INC.

New York, N.Y.
Booth 212

Fellows Medical Manufacturing Co., Inc. cordially invites you to visit their booth where representatives will be glad to discuss such new products as ArleC suppositories, Aminophylline-Barbiturate Compound for prompt relief and rest in asthmatic conditions; EQUIL liquid and tablets (enteric coated)—Sodium Salicylate and Menadione for safer salicylate therapy; IONLEX with FOLIC ACID TABLETS containing Ferrous Gluconate, Liver, Vitamin B-Complex and Vitamin C for secondary anemias; FELLO-SOL, Calcium Sedative Elixir containing Chloral Hydrate, Calcium Bromide and Atropine Sulfate in a palatable sugar-free vehicle.

H. G. FISCHER & CO.

Chicago, Ill.
Booth 79

Visitors will be welcome at Booth 79 where H. G. Fischer & Company will display modern units of X-Ray and Physio-Therapy equipment including models of F. C. C. Type Approved Diathermy Apparatus with the patented induction electrode. Factory trained representatives will be pleased to demonstrate this equipment without obligation.

C. B. FLEET COMPANY, INC.

Lynchburg, Va.
Booth 102

C. B. Fleet Co., Inc. cordially invites you to visit Booth 102. Increasingly, during the past fifty years, to the medical profession, sodium phosphate has come to mean Phospho-Soda (Fleet), the pure, stable, aqueous concentrate of the two U.S.P. sodium phosphates.

FOLEY MANUFACTURING CO.

Minneapolis, Minn.
Booth 104

You are invited to stop at our exhibit. Our representative will be delighted to show you the Baby Size Foley Food Mill, which is just back on the market. It is especially designed for straining individual portions of food for all smooth diets.

GARDNER MANUFACTURING COMPANY

Horicon, Wis.
Booth 179

The Gardner Manufacturing Company has devoted much time the past two years experimenting with an item which, when finished, will remove at least two hours of drudgery a day from hospital personnel, thereby freeing them for greater efforts in other directions. It is hoped a sample of this revolutionary product will be available for a Premier showing at the Cleveland meeting, but nevertheless, the famous Gardner Radiator Enclosures, Ice Chests, Bedside Tables and Storage Cabinets will be exhibited.

GERBER PRODUCTS COMPANY

Freemont, Mich.
Booth 130

Gerber Products Company cordially invites you to visit them and sample the display of their new Strained and Junior Meats for Babies. Both textures are available in beef, veal and liver. Informational literature on prenatal and child care and feeding, analytical data and adult special diet uses of strained foods and cereal samples are available.

OTIS E. GLIDDEN & CO., INC.

Evanston, Ill.
Booth 215

Zymenol, an emulsion with Brewers' Yeast, provides an effective bowel management routine without irritant, habit-forming drugs or bulking agents. Visit the Glidden booth and sample the new Zymenol. A new process assures a fine, creamy-white emulsion with exceptional stability and palatability. Descriptive literature and trial supply available. Convince yourself.

GRADWOHL LABORATORIES

St. Louis, Mo.
Booths 223-224

This organization will show its various activities: Training of laboratory technicians; manufacturing of laboratory reagents; publication of a monthly journal called the *Laboratory Digest* and the fourth edition of Gradwohl's textbook *Clinical Laboratory Methods and Diagnosis*, published by the C. V. Mosby Company. Of particular interest will be the demonstration of the Papanicolaou method, stains, etc.

GRUNE & STRATTON, INC.

New York, N.Y.
Booth 174

Outstanding among new publications for postgraduate

teaching to be displayed include: Neuhof—*Venous Thrombosis in Pulmonary Embolism*; Moschowitz—*Biology of Disease*; Daley and Miller—*Progress in Clinical Medicine*; Hill and Dameshek—*Rh Factor in the Clinic and Laboratory*; Dameshek and Estren—*Spleen and Hypersplenism*; Hoch—*Failures in Psychiatric Treatment*; Wolberg—*Medical Hypnosis* (Volume I, Principles of Hypnotherapy; Volume II, Practice); the 1948 volume of the well known *Progress in Neurology and Psychiatry* edited by Spiegel, and Bellak's *Dementia Praecox*.

HAMILTON MANUFACTURING COMPANY

Two Rivers, Wis.
Booths 88-89-90

Three suites of Examining Room Furniture will be displayed: Deluxe Nu-Tone, the distinctive and modern Nu-Trend and the professionally styled Steeltone. Also shown will be the No. 9905-B-AP All-Purpose Examining Chair-Table, the No. 9595 EENT Cabinet, the representative items of business office and reception room furniture.

HANOVIA CHEMICAL & MANUFACTURING CO.

Newark, N. J.
Booth 227

Don't fail to visit our booth. A complete line of ultra-violet equipment for official and general body radiation will be on display, also radiant heat lamps, Germicidal Lamps for the destruction of air-borne bacteria and the new Short Wave Diathermy.

CHR. HANSON'S LABORATORY, INC.

"JUNKET" BRAND FOODS
Little Falls, N. Y.
Booth 7

The importance of rennet in infant and adult nutrition and the value of rennet desserts in both normal and restricted diets will be explained. Enlarged photos illustrate the action of the rennet enzyme in producing softer, finer, more readily-digestible milk curds. Authoritative literature is available describing dietary applications of rennet products. Complimentary packages of "Junket" Rennet Powder and "Junket" Rennet Tablets for the profession.

HARROWER LABORATORY, INC.

Glendale, Calif.
Booth 30

The Harrower technical exhibit presents gastroscopic and acidity control studies relative to Mucotin, a new treatment for peptic ulcer. Proof of the coating action of Mucotin is presented with illuminated gastroscopic pictures. A case history report of a healed gastric ulcer is also illustrated gastroscopically. Mucotin is accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

H. J. HEINZ COMPANY

Pittsburgh, Pa.
Booth 211

The H. J. Heinz Company would like you to taste and see all their tin-packed Strained and Junior Foods. Highly fortified Pre-Cooked Cereal Food and Pre-Cooked Oatmeal are on display, too. Our well-known Nutritional Charts, other nutrition information and literature on Heinz Baby Foods are available.

PAUL B. HOEBER, INC.

New York, N. Y.
Booth 59

PAUL B. HOEBER, INC., Medical Book Department of Harper & Brothers, invite you to inspect the entire list of HOEBER publications including these new volumes for the family physician: the new fourth edition of Alvarez' *Introduction to Gastro-Enterology*, Barrow's *Clinical Management of Varicose Veins*, Mengert's *Postgraduate Obstetrics*, and Schwedel's *Clinical Roentgenology of the Heart*. The valuable *Modern Trends* series will be represented by the new MacKenna's *Dermatology*, Sorsby's *Ophthalmology* and McLaren's *Diagnostic Radiology*. Late issues of the Hoeber journals, *Cancer* and *Psychosomatic Medicine* will also be available. Be sure to visit the Hoeber booth.

HOFFMANN-LA ROCHE, INC.

Nutley, N. J.
Booth 75

Roche is happy to exhibit at the meeting of the Interstate Postgraduate Medical Association. They invite all members of the Association to visit Booth 75 where members of the representative staff will be present to discuss such new products as SYRUP SEDULON, a sedative cough preparation especially useful for night cough; THEPHORIN, a different antihistamine which is not likely to cause drowsiness; PRESIDON, the mild new sedative-hypnotic which is not a barbiturate and does not cause "hangover."

HOLLAND-RANTOS COMPANY, INC.

New York, N. Y.
Booth 187

You are cordially invited to register at this booth to receive professional samples of NYLMERATE JELLY, a specific, convenient and inexpensive treatment for trichomonas vaginitis, nonspecific vaginal discharges, and for use in postcauterization therapy. Also on exhibit you will find Koromex Diaphragm Fitting Rings for prescribing the KOROMEX METHOD when conception control is indicated, along with Council-Accepted Koromex Jelly and Cream, Koromex Sets Complete and the different types of Koromex Diaphragms.

HOLLISTER-STIER LABORATORIES

Wilkinsburg, Pa.
Booth 200

In the spotlight at Booth 200 is the new lucite plastic case accommodating an improved integral dropper vial for diagnostic allergens. With allergy an important part of all types of practice, a visit to the home of PERSONALIZED ALLERGY SERVICE will be a must. Ask for your copy of the new booklet, "Ready Reference Reader on Allergy." Trained representatives will be happy to give you information and discuss the complete allergy service of Hollister-Stier Laboratories.

IRWIN, NEISLER & COMPANY

Decatur, Ill.
Booths 18-19

New clinical information on the use of Vertavis in the treatment of severe and resistant hypertension will be presented. Our medical service representatives will be in attendance to give any information desired. Physicians are welcome to visit our Exhibit.

JOHNSON & JOHNSON
New Brunswick, N. J.
Booths 142-143

Hemo-Pak Hemostatic Absorbable Surgical Dressings will be featured at the J & J booths. Representatives also extend a welcome to you to discuss Johnson & Johnson's new, improved adhesive tape, Johnson's Baby Lotion, or to just "visit."

JONES METABOLISM EQUIPMENT CO.
Chicago, Ill.
Booth 100

A special feature at this exhibit will be the new JONES SUPER-MOTOR-BASAL metabolism unit. Trained technicians will demonstrate how this custom-tailored unit, built with a large breathing chamber for large patients and irregular breathers, inside of which is a smaller breathing chamber for smaller patients, operates as "Two-Machines-In-One." With this unit the most extreme cases can be handled with greater precision and minimum of time and special effort.

JORDAN PUMP COMPANY
Kansas City, Mo.
Booth 197

Booth 197 will show and demonstrate 3½ pound motor driven pump Unit for Penicillin Mist, replacing need of heavy oxygen equipment. Showing and demonstrating pressure and vacuum pump Unit equipped with special flutter valve to positively control negative pressure within the head, permitting Mist to enter sinus cavities when open, using only negative pressure. This method mechanically creates mild massage within the head, eventually breaking crust which forms over sinus openings.

THE KELLEY-KOETT MANUFACTURING CO.
Covington, Ky.
Booths 145-146

The Keleket KXP Combination, finished in handsome Keleket, is being shown. It is the most complete and compact Diagnostic X-Ray Unit, combining radiographic and fluoroscopic facilities plus facilities for any diagnostic requirements needed by the general practitioner, clinic and small hospital. See this moderate priced unit demonstrating the efficiency and pointing out its many features designed to simplify the required steps in radiographic and fluoroscopic procedures. A complete line of x-ray accessories and supplies are also available.

KIDDE MANUFACTURING CO., INC.
Bloomfield, N. J.
Booths 71-72

In Booth 71 the new KIDDE-Utero Tubal Insufflator with GASOMETER pressure control. Completely safe—gravity pressure control—simple operation—single control. Requires only small cartridge of carbon dioxide gas. Provides diagnostic and therapeutic use of carbon dioxide gas or opaque oil. Kymographic record of patency test. Also on display the KIDDE Dry Ice Apparatus used in treatment of superficial skin lesions. This apparatus is becoming increasingly popular because of its simplicity and superior cosmetic results obtained.

CHARLES B. KNOX GELATINE COMPANY
Johnstown, N. Y.
Booth 166

The exhibit of the Charles B. Knox Gelatine Company

features the medical and dietary uses of Knox Plain Sparkling Gelatine. Attendants will gladly discuss the protein value of gelatine and explain how the production and laboratory control makes Knox Gelatine a quality product, helpful in special dietary cases. Literature, including dietaries and recipes, is free.

LAKESIDE LABORATORIES, INC.
Milwaukee, Wis.
Booth 179A

The Lakeside Exhibit will feature the mercurial diuretic, MERCURYDRIN. Representatives will be on hand to describe the use of this modern diuretic in early and late cardiac decompensation and other conditions. This, as well as other Lakeside specialties which will be displayed, have created general interest and medical discussion this year.

LANTEEN MEDICAL LABORATORIES, INC.
Chicago, Ill.
Booth 128

Lanteen Medical Laboratories, Inc. extend a cordial invitation to visit Booth 128. Featured will be the well known Lanteen Flat Spring Diaphragm, and representatives will be pleased to discuss the new and improved diaphragm technic.

LEA & FEBIGER
Philadelphia, Pa.
Booth 83

Lea & Febiger invites you to stop and examine their selection of new books and new editions, including Ormsby and Montgomery—*Diseases of the Skin*; Gray—*Anatomy of the Human Body*; Frohman—*Brief Psychotherapy*; Partipilo—*Surgical Technic and Principles of Operative Surgery*; Herbut—*Surgical Pathology*; Spaeth—*Principles and Practice of Ophthalmic Surgery*; Krinsky—*Binocular Imbalance*; Kraines—*Therapy of the Neuroses and Psychoses*; Burch and Reaser—*Primer of Cardiology*, and many other books of practical help and guidance.

LEDERLE LABORATORIES DIVISION
AMERICAN CYANAMID COMPANY
New York, N. Y.
Booths 120-121

You are cordially invited to visit our exhibit where you will find representatives who are prepared to give you the latest information on Lederle products.

LIEBEL-FLARSHEIM COMPANY
Cincinnati, O.
Booth 216

The Liebel-Flarsheim Company cordially invites you to stop for examination and demonstration of their latest model diathermy and Bovic electrosurgical equipment. Capable representatives will be on hand at all times to answer your questions about physical therapy and electrosurgical apparatus. We hope you will stop by so that we may become acquainted.

ELI LILLY AND COMPANY
Indianapolis, Ind.
Booths 123-124-125

Featured at the Lilly exhibit will be new therapeutic developments and a demonstration of the Blood Sugar Screening Test (Wilkinson-Helfmann Method). This new test takes only five minutes to perform, is accurate within 5 mg. per cent of true glucose value and requires but 0.1 cc. of

blood. No preparation, standardization, pipetting, titration, or distilled water is necessary. Your Lilly medical service representative cordially invites you to visit the Lilly exhibit.

J. B. LIPPINCOTT COMPANY
Philadelphia, Pa.
Booths 53-54

J. B. Lippincott Company presents an interesting and active exhibit of professional publishing. With the "pulse of practice" centering in an advisory editorial board of active clinicians who constantly review the field, current and coming trends in medicine and surgery are known continually. On the studied recommendations of these medical leaders, Lippincott Selected Professional Books are undertaken. It is upon their knowledge too, of the outstanding work being done in general practice, as well as specialties, that men making a very real contribution to medical progress are chosen to author the Lippincott books.

LLOYD BROTHERS, PHARMACISTS, INC.
Cincinnati, O.
Booth 193

Lloyd Brothers will present a group of new specialty products derived largely from botanical sources. Each is a unique preparation, well established through clinical study, and prepared by the patented Lloyd extraction process. Essential hypertension, allergy, general congestion and biliary dysfunction are among the fields of treatment explored with Lloyd products.

M & R DIETETIC LABORATORIES, INC.
Columbus, O.
Booth 150

M & R Dietetic Laboratories, Inc. will display Similac, a food for infants deprived either partially or entirely of breast milk. Messrs. D. O. Cox, J. J. Quilligan, A. M. Huber, H. W. Sackett, E. M. Smith, L. A. MacDonald, and R. L. Wilson will appreciate the opportunity to discuss the merit and suggested application for both the normal and special feeding cases.

THE MACMILLAN COMPANY
New York, N. Y.
Booth 129

Psychiatry in a Troubled World, a new book by Dr. William C. Menninger of the Menninger Foundation, will be offered by Macmillan. "Yesterday's war" from the psychiatric standpoint and "today's challenge"—a plea for application of psychiatric measures to prevent perplexing problems—is discussed. *Glomerular Nephritis* (Macmillan), containing Dr. Thomas Addis' method of diagnosing and treating Bright's disease will interest the general practitioner.

THE MAICO COMPANY, INC.
Minneapolis, Minn.
Booth 201

The Maico Exhibit will feature Maico's electronic stethoscope—the Stethetron. With the selective amplification of this instrument, the physician can amplify the sounds he is particularly interested in and, at the same time, subdue the other body sounds. This is the first real advance in diagnosis by auscultation in one hundred years and it is well worth your time to see and try this instrument.

MALTBIE CHEMICAL COMPANY
Newark, N. J.
Booth 177

Selective oral therapy in hepato-biliary disease will be the main feature of the Maltbie exhibit. Trained representatives will be present to explain the applications of Cholan-DH and Cholanox as well as other Maltbie specialties. Special requests will receive immediate attention. All physicians and guests are cordially invited to attend.

THE MALTINE COMPANY
Morris Plains, N. J.
Booth 5

Learn about the newer MALTINE specialties in a few minutes. Representatives will be on hand with samples and literature describing recent MALTINE firsts—the first bulk laxative in tablet form—the first true amino acid tablet—the newer THROMBOPLASTIN diagnostic agent—the new rectal ointment containing natural mucin. PROLOID, TEDRAL and DEPANCOL will be featured also at the MALTINE exhibit.

F. MATTERN MANUFACTURING CO.
Chicago, Ill.
Booth 186

A visit to the Mattern Booth will enable you to personally examine one of Mattern's many well known modern X-Ray Units. The unit on display is a single tube, hand tilt table unit with Deluxe Push Button Control finished in a beautiful Ivory Finish. Your inspection is welcomed and further information will be available upon your visit to our booth.

McNEIL LABORATORIES, INC.
Philadelphia, Pa.
Booth 77

The new chemotherapeutic preparation—LIQUID MER-DIAZINE—is presented by means of displays which point out the factor of safety in use. Mer-Diazine combines sulfamerazine microcrystalline and sulfadiazine microcrystalline in the unusual Liquoid dosage form. Also on exhibit will be recent facts about Butisol Sodium—the "Intermediate Sedative-Hypnotic." Physicians are invited to discuss the unusual factors of these two new preparations with our representatives who will be in attendance.

MEAD JOHNSON & COMPANY
Evansville, Ind.
Booths 167-168

Amigen and Protolysate will be on display at the Mead Johnson Exhibit at your I.P.M.A. meeting. Mead Johnson has pioneered the amino acid field commercially; the products have been described in more than one hundred and forty articles in the medical literature; this year they are available. Trained representatives will be at the Mead Exhibit to discuss details of the new amino acid products. Shown also will be Dextri-Maltose, Pabulum, Pabena, Oleum Percomorphum and the other Mead products used in Infant Nutrition. Protenum, a new high-protein product, will be displayed. Also Lonalac for low-sodium diets.

MEDICAL CASE HISTORY BUREAU
New York, N. Y.
Booth 60

An inexpensive case history method. A system which shows at a glance the case you want, how many calls you made and when, the patient's history, developments and treatments, as well as the financial status of each case. The

Medical Case History Bureau has specialized for many years in record forms for the doctor's office. Their well informed representatives will gladly demonstrate the Info-Dex System and discuss your office problems.

MEDICAL FILM GUILD

New York, N. Y.
Booths 183-184-185

Medical Film Guild, through MEDICAL FILMS THAT TEACH, presents a refresher course in fundamental medical problems. Each film subject is produced in the manner of a textbook, profusely illustrated, offering information comparable to that found in postgraduate courses as presented at our leading medical schools. These films review such subjects as Occupational Health Problems, Management of the Failing Heart, Hypothyroidism, Arterial Blood Pressure, The Major Neuralgias, A Clinic on Deafness, Cervicitis, Parkinson's Disease, Otitis Media in Pediatrics, Mastoiditis, Sinusitis, Trichomoniasis and Moniliasis, and many others.

MERCK & COMPANY, INC.

Rahway, N. J.
Booths 154-155

The Merck Exhibit is devoted to the important subject of streptomycin with emphasis on its role in the treatment of tuberculosis. X-rays taken before and after the use of streptomycin in patients with the following types of tuberculous lesions are on display: Patient A—Advanced caseous tuberculous tuberculosis in a diabetic; Patient B—Advanced pulmonary tuberculosis and tuberculous pyopneumothorax; Patient C—Advanced pulmonary and laryngeal tuberculosis; Patient D—Acute primary pulmonary and ulcerative oropharyngeal tuberculosis. Another use of streptomycin referred to in the display is in the treatment of gonorrhea. Other Merck preparations on display will be Neo-Antergan—a remarkably efficient histamine antagonist of low toxicity; Vinethene—the inhalation anesthetic for short procedures; Crystalline Penicillin G Sodium, and Myochrysin for the treatment of active rheumatoid arthritis.

THE WM. S. MERRELL COMPANY

Cincinnati, O.
Booths 23-24

Mercodol, the new antitussive syrup containing the better cough-controlling narcotic, Mercodionone, will be featured by Merrell. Mercodionone, a better antitussive agent than either heroin or codeine, is notably free from the undesirable side effects of the older drugs. Mercodol also contains the bronchodilator, Nethamine, and the saline-expectorant, sodium citrate.

THE C. V. MOSBY COMPANY

St. Louis, Mo.
Booth 37

A cordial invitation is extended all physicians attending the Assembly of the I.P.M.A., to visit the C. V. Mosby Company display, where a wealth of new and timely medical literature will be available for examination. Some of the very new releases to be shown will include Crossen—*Operative Gynecology*; Pottenger—*Tuberculosis*; Gradwohl—*Clinical Laboratory Methods and Diagnosis*; Dunbar—*Synopsis of Psychosomatic Diagnosis and Treatment*; Watson—*Hernia*, and Willis—*Pathology of Tumors*.

V. MUELLER & COMPANY

Chicago, Ill.
Booths 28-29

Many of the most recent developments in instruments for modern surgical techniques will be featured in the exhibit of V. Mueller & Company. The display will also include a broadly representative selection from the complete Mueller line of standard and special instruments and equipment for every field of surgical practice.

THE NATIONAL DRUG COMPANY

Philadelphia, Pa.
Booth 55

RESINAT, the resin antacid for the treatment of peptic and duodenal ulcers, will be the featured product at the booth of The National Drug Company. You are cordially invited to visit our booth where trained representatives will be available to explain the efficacy and discuss the therapeutic values of this new antacid. Other ethically promoted products manufactured by this company will be displayed and detailed.

WHITTIER LABORATORIES

DIVISION NUTRITION RESEARCH
LABORATORIES

Chicago, Ill.
Booth 173

A friendly welcome awaits you at the Whittier Laboratories exhibit which features: ETRON—Steroid Complex, Whittier, for the treatment of arthritis; ARZON—Whole vitamin B complex plus vitamin C; INFON Pediatric—For rickets prophylaxis; PENARVON—A palatable, balanced source of the essential amino acids and vitamins of the B complex; and LACTUM—The effective hematinic for hypochromic or nutritional anemia.

ORTHO PHARMACEUTICAL CORPORATION

Raritan, N. J.
Booth 65

Ortho cordially invites you to visit Booth 65 where they will exhibit their gynec specialties, including Ortho-Gynol and Ortho-Creme. Also on display will be newer products for the treatment of vaginal infections and other gynecologic and obstetric problems. Well trained representatives will be on hand to discuss these products with interested physicians.

ORTHOPEDIC FRAME COMPANY

Kalamazoo, Mich.
Booth 228

The Orthopedic Frame Company will feature the new Stryker Bone Saw. This electrically driven, oscillating type safety bone saw cuts bone efficiently with no danger to the patient or surgeon. Also displayed will be the proved Stryker Cast Cutter and the reliable Stryker Turning Frame with its latest improvements.

PARKE, DAVIS & COMPANY

Detroit, Mich.
Booths 95-96-97-98

The Parke, Davis & Company exhibit features ETAMON chlorure which temporarily blocks the transmission of nerve impulses at the autonomic ganglia. Pharmacologic and physiologic effects on the vascular and gastrointestinal systems are shown. As the drug is indicated as a diagnostic or therapeutic agent, where sympathectomy may be of bene-

fit, the conditions wherein it has been used are portrayed. You are cordially invited to call at our Exhibit with the assurance your interest will be appreciated.

THE E. L. PATCH COMPANY

Boston, Mass.

Booths 68-69

The E. L. Patch Company exhibit will interest every physician because it will feature Glytheonate (Patch), the new theophylline sodium glycinate product for intensive theophylline therapy in the treatment of cardiac asthma and coronary occlusion. In addition, there will be exhibited other Patch products, including Kondremul, Gadoment, Trydecyl and Predaten. Patch representatives will be on hand to serve you.

PET MILK COMPANY

St. Louis, Mo.

Booths 86-87

An actual working model of a milk condensing plant in miniature will be exhibited by the Pet Milk Company. This exhibit offers an opportunity to obtain information about the production of Pet Milk, its use in infant feeding, and the time-saving Pet Milk services available to physicians. Miniature Pet Milk cans will be given to the physicians who visit the Pet Milk booth.

PHILIP MORRIS & CO. LTD., INC.

New York, N. Y.

Booth 137

Philip Morris & Company will demonstrate the method by which it was found that Philip Morris Cigarettes, in which diethylene glycol is used as the hygroscopic agent, are less irritating than other cigarettes. Their representative will be happy to discuss researches on this subject, and problems on the physiologic effects of smoking.

PICKER X-RAY CORPORATION

New York, N. Y.

Booths 91-92

Picker X-Ray Corporation will display the SERIES "200" with Spot Film Device and the New Electronic V-7 Control providing Fully Automatic Selection of Technic. There will also be on display the new GYNOGRAPH for the diagnosis and treatment of female sterility.

PIONEER RUBBER COMPANY

Willard, O.

Booth 76

The Pioneer Rubber Company will feature the following: ROLLPRUF Surgical Gloves of Latex and Neoprene; QUIXAMS, the short glove for dressings and examinations; Obstetrical Gloves and Heavy Duty Utility Gloves.

PITMAN-MOORE COMPANY

Indianapolis, Ind.

Booths 47-48

The Pitman-Moore display will feature a number of products developed by the Company's research department, including Magmoid Sulfadiazine, a Council-Accepted dosage form of fluid sulfadiazine; Magmoid Sulco, a triple sulfonamide in fluid form; and the new Ultraviolet-Irradiation Killed Rabies Vaccine. Experts from the Pitman-Moore scientific staff will be on hand to answer technical questions.

PLASTISHIELD, INC.

Minneapolis, Minn.

Booth 214

PLASTISHIELDS, shaped plastic shields, represent a new

technic for the ante and postpartum care of the breast and nipple and was inspired by the need for a technic which would attack the unfortunately high incidence of nursing difficulties arising from cracked, sore, bleeding nipples, and breast infections. The PLASTISHIELD technic is now an established routine in many hospitals throughout the United States and Canada. With this technic, time required of maternity nurses in assisting the nursing mother is greatly reduced. PLASTISHIELDS are used without any medication. Trained nurses will be available at our exhibit to explain this technic.

POLORIS COMPANY, INC.

Jersey City, N. J.

Booth 195

The Poloris Company's exhibit will provide the visiting members with literature and professional samples of Poloris Dental Poulitice. Poloris is an ethically promoted local medicinal counterirritant widely prescribed by the dental profession for the relief of pain and soreness due to irritation of teeth and gums.

W. F. PRIOR COMPANY

Hagerstown, Md.

Booth 78

PROFESSIONAL EQUIPMENT COMPANY

Chicago, Ill.

Booths 139-140

The exhibit of the Professional Equipment Company will feature the new Vertical Fluoroscopy Attachment recently developed for the Profexray Table Combination Radiographic and Fluoroscopic Unit. This attachment synchronizes the travel of the screen and powerhead, both vertically and horizontally, with the patient standing or seated at the end of the table. Other Profexray Units which will be exhibited include the Vertical Combination, the Mobile and Portable Units.

RARE CHEMICALS, INC.

Harrison, N. J.

Booth 99

New preparations in Rare's exhibit include: (1) Terjolate, companion product to Acidolate and Dermolate, skin detergents. Terjolate is a soapless, hypoallergenic, nonirritating detergent for dishwashing and general household cleansing. (2) Dienestrol "Rare," well tolerated and economical estrogenic preparations, now also available in aqueous suspension form for injection. Other Rare products to be displayed are: Rare's male hormone preparations for oral, parenteral and sublingual use; Salysal, salicylate which requires no alkali, Progesterone "Rare" and Chorionic Gonadotropin "Rare."

REED & CARNRICK

Toronto, Ont., Canada

Booths 57-58

Meprane Dipropionate, an entirely new synthetic estrogen for oral administration, is presented. Impressive clinical studies, reported in a leading medical journal, add to the rapidly accumulating evidence of the clinical efficacy of this preparation. Estrogenic Substances, R & C (formerly Estrogenic Hormones, R & C), a highly potent, clinically dependable mixture of natural estrogens, is also presented. Estrogenic Substances, R & C, is one of the most widely used preparations of its kind. It is available in oil solution and in a sterile aqueous suspension for parenteral administration.

J. B. ROERIG AND COMPANY
Chicago, Ill.
Booth 147

Attending physicians are cordially invited to attend the exhibit of J. B. Roerig and Company. Members of the Professional Service Department will be on hand to explain in detail the several products which will be displayed. Three new products will be featured: Heptuna with Folic Acid, a combination of ferrous sulfate, essential vitamins and folic acid; Obron, a new di-calcium phosphate, iron and vitamin capsule; and Lactenz, a protein hydrolysate. Company representatives will welcome all inquiries and will be pleased to extend the courtesy of the Professional Service Department to all visitors.

RYSTAN COMPANY, INC.
Mount Vernon, N. Y.
Booth 63

CHLORESIUM Preparations contain the water-soluble derivatives of Chlorophyll "a" ($C_{55}H_{72}O_5N_4Mg$). They are natural, nontoxic biogenic healing agents indicated in the topical treatment of wounds, burns, ulcers, dermatoses, and similar lesions; also for treating acute and chronic inflammatory conditions of the upper respiratory tract and oral cavity. These cell-stimulating, biotherapeutic preparations also promptly deodorize malodorous conditions.

SANBORN COMPANY
Cambridge, Mass.
Booth 64

On exhibit will be three completely new developments in instruments for cardiac diagnosis and research: The Sanborn Electromanometer, for direct recording of blood pressures (venous and arterial), intracardiac and spinal pressures, etc.; the "Poly-Viso," a two-to-four channel recorder for electrocardiograms, blood pressures, sphygmogram, electrokymogram, ballistocardiogram and other phenomena; and the Sanborn Electrokytograph. Also on display will be the popular Sanborn instruments for clinical use: the Viso-Cardiette, the Instamatic Cardiette, and the new Sanborn Metabolism Tester—the Metabulator.

SANDOZ CHEMICAL WORKS, INC.
New York, N. Y.
Booths 25-26

Among recently released Sandoz Medicinal Specialties are: MELSANTON (methyl-phenyl-ethyl-hydantoin), anti-epileptic for the control or reduction in the frequency of epileptic seizures; Dihydroergotamine "Sandoz" (D.H.E.-45), the improved non-narcotic relief for migraine; Glysenid for constipation—contains the crystalline glycosides from senna leaves, Sennosides A and B; also displayed are Cedilanid, stable preparation of Lanatoside C, a crystalline glucoside from Digitalis Lanata, not present in purpurea; Ipsandrine Syrup for the relief of cough and bronchial disorders—containing the active alkaloids of Dover's Powder in pure form with ephedrine.

W. B. SAUNDERS COMPANY
Philadelphia, Pa.
Booths 42-43

This Company will exhibit their full line of medical books including Hyman's *Integrated Practice of Medicine*, Blockus' *Gastro-enterology*, Kinsey's *Sexual Behavior in the Human Male*, Sollmann's *Pharmacology*, Beckman's *Treat-*

ment, Todd & Sanford's *Clinical Diagnosis by Laboratory Methods*, Christopher's *Minor Surgery*, DeGowin, Hardin & Alsever's *Blood Transfusion*, Snyder's *Obstetric Analgesia*, Long's *A B C's of Sulfonamide and Antibiotic Therapy*, Dowling's *Acute Bacterial Diseases*, Noyes' *Clinical Psychiatry*, Brams' *Treatment of Heart Disease*, A.M.A. *Interns Manual*, Thorner's *Psychiatry in General Practice*, Wechsler's *Clinical Neurology*, and many others.

SCHENLEY LABORATORIES, INC.
New York, N. Y.
Booth 127

The Schenley Laboratories' exhibit features standard penicillin products, Penicillin Vaginal Suppositories, Rutaminal, and Titrulac. RUTAMINAL TABLETS are an exclusive Schenley specialty supplying rutin, aminophylline, and phenobarbital. TITRULAC, another Schenley specialty, is a particularly palatable antacid with a titration curve resembling that of milk. Well informed personnel in attendance.

SCHERING CORPORATION
Bloomfield, N. J.
Booths 188-189

Among the new pharmaceutical and hormone preparations developed in the Schering research laboratories, MICRO-PILLETS PROGYNON will be featured. This new potent form of the female sex hormone, alpha estradiol, provides maximum results at minimum cost to the patient. COMBISUT and COMBISUT LIQUID, the triple sulfonamide combinations which eliminate the dangers of sulfonamide renal damage will also be presented. TRIMETON, the completely new antihistaminic will highlight the exhibit. Schering Professional Service Representatives will be present to welcome you and will be happy to answer your inquiries concerning Schering's new products as well as their other hormone, x-ray diagnostic, chemotherapeutic, and pharmaceutical specialties.

JULIUS SCHMID, INC., GYNECOLOGICAL DIVISION
New York, N. Y.
Booths 113-114

Physicians may see how a prescription for the correct size RAMSES Prescription Packet #501 will supply the patient optimum protection with simplicity in use. Reproductions of roentgenographs and drawings in color show how the examining physician can questionably fit the patient. Representatives will welcome questions regarding RAMSES Gynecological Products—every one Council Accepted. These are RAMSES Flexible Cushioned Diaphragm, RAMSES Diaphragm Introducer, RAMSES Vaginal Jelly, RAMSES Vaginal Applicator and RAMSES Fitting Rings.

SEAMLESS RUBBER COMPANY
New Haven, Conn.
Booth 204

The Seamless Rubber Company will display a new booth which will feature Seamless PRO-CAP, the new adhesive plaster which minimizes irritation and itching. PRO-CAP, the only adhesive plaster containing the fatty acid salt—zinc propionate and zinc caprylate. In the display will be six Kodachromes showing actual samples of application of PRO-CAP and ordinary adhesive plaster. Seamless STANDARD SURGEONS' GLOVES will also be featured as will Seamless EASYWEAR NURSE. Seamless line of medical rubber goods and surgical dressings will also be shown.

G. D. SEARLE & COMPANY
Chicago, Ill.
Booths 8-9-10

You are cordially invited to visit the Searle booth where our representatives will be happy to answer any questions regarding Searle Products of Research. Featured will be Ruphyllin, for abnormal capillary fragility, Hydryllin, new and effective antihistaminic, as well as such time-proved products as Searle Aminophyllin in all dosage forms, Metamucil, Ketochol, Floraquin, Kiophyllin, Diodoquin, Pavatrine and Pavatrine with Phenobarbital.

SHAMPAINE COMPANY
St. Louis, Mo.
Booths 229-230

On display at this booth will be the Perfection Major Operating Table, which features completely head-end controls, and ease of operation. Also on display will be a complete assembly of metal and hydraulic equipment for the physician's office, as well as furniture suitable for use in reception room. Trained representatives will be on duty at all times.

SHARP & DOHME, INC.
Philadelphia, Pa.
Booths 38-39-40-41

Sharp & Dohme extends a cordial welcome to all visitors. Products on exhibit include "Staticin" Caronamide, the new compound that permits smaller penicillin dosage and provides more effective blood levels; Blood Group Specific Substances A & B for conditioning group O blood to eliminate a potential source of transfusion reactions; "Delvinal" Sodium Vinbarbital, for the production of obstetric amnesia and analgesia; "Delcos" Granules, an exceptionally palatable protein agent; new antibiotic preparations including "Tyrozets" Antibiotic-Anesthetic Throat Lozenges, "Prothricin" Antibiotic Nasal Decongestant, and "Tyroderm" Tyrothricin Cream. "Sulfathalidine" and "Sulfasuxidine" complete the products on exhibit.

SIEBRANDT MANUFACTURING CO.
Kansas City, Mo.
Booth 219

The Siebrandt Mfg. Co. will display a number of new Instruments. They will show the new Improved Jackson Bone Clamp for reduction and alignment of fractures, especially of femurs. The outstanding feature of the Exhibit will be a Plate Holding Clamp, designed by Siebrandt. This Bone Clamp presents an entirely new approach in the technique of applying bone plates. The jaws are so designed that after applying them over the fragments and immobilizing the fracture, the Bone Plate is then easily inserted and held against bone surface by means of a set screw. They will also show a new Drill Guide which assures accurately centered holes, and the Removable Plaster Hitch set.

J. SKLAR MANUFACTURING CO.
Long Island City, New York, N. Y.
Booth 165

J. Sklar Manufacturing Co. this year presents a comprehensive display of Stainless Steel Surgical Instruments, many of which are new and have never before been displayed before an I.P.M.A. Convention. The new instruments were designed, developed and manufactured in cooperation with leading American Surgeons. The display also includes Sklar's full line of Suction and Pressure Apparatus, long known and recognized for perfect performance.

ance. Ask to see Sklar's Improved Schiotz Tonometer, and the popular Davidson's Pneumothorax Apparatus.

THE SMITH-DORSEY COMPANY
Lincoln, Nebr.
Booth 138

Injectable and oral preparations will be featured at The Smith-Dorsey exhibit. Al-Si-Cal Powder and Tablets, which are specifically designed for the ulcer patient will be shown. Teotine Tablets for chronic heart conditions will be on display, and Ilban Capsules for secondary anemias and general tonic purposes will also be exhibited. The injectable material will cover a wide range of Council Accepted items which will be of interest to all physicians engaged in internal medicine. The Dorsey representatives welcome all physicians to their booth each day of the meeting.

SMITH, KLINE & FRENCH LABORATORIES
Philadelphia, Pa.
Booths 170-171

"DEXEDRINE" SULFATE (Dextro-amphetamine sulfate, S.K.F.): "Dexedrine" therapy—now established as the treatment of choice in overweight—spares the patient the discouragement and irritability which ordinarily accompany adherence to reducing regimens. Because it successfully curbs appetite, "Dexedrine" makes it easy for the overweight patient to stop overeating. Thus it reduces weight safely—without the use (and risk) of such drugs as thyroid.

SPENCER, INCORPORATED
New Haven, Conn.
Booth 163

You are cordially invited to visit our exhibit of Spencer Individually Designed Supports for abdomen, back, and breasts. The Spencerflex, a light, comfortable, masculine-looking support for men, will be featured. This support improves posture, increases efficiency and helps prevent hernia. It is especially suited for postoperative wear. Another support displayed will be the Spencer Sacroiliac Corset, designed to limit movement of the sacroiliac joints to relieve pain caused by sacroiliac sprain. The Spencer Breast Form, which conceals disfigurement and restores normal figure lines for the mastectomy patient, will also be shown.

E. R. SQUIBB & SONS
New York, N. Y.
Booths 51-52

E. R. Squibb & Sons will feature Crysticillin, the new procaine penicillin G for aqueous injection with other antibiotic agents.

R. J. STRASENBURGH CO.
Rochester, N. Y.
Booth 203

The R. J. Strassenburgh Company exhibit will feature the results of research and investigation in three fields—Cardiology, Gastroenterology and Dermatology.

STRONG COBB AND COMPANY, INC.
Cleveland, O.
Booth 182A

New scientific automatic ampule injector, the AMPIN, for subcutaneous injection. For speedy injection of emergency drugs. Entirely eliminates usual hypodermic procedure. Saves doctor's time, is easy and convenient to use. Nothing to dissolve, sterilize or assemble. AMPINS are completely sterile, tamper-proof and low cost. See AMPINS demonstrated and try them for yourself.

TECHNICAL EXHIBITS

SUTLIFF & CASE CO., INC.
 Peoria, Ill.
 Booths 44-45

Sutliff & Case Co., Inc. is always happy to exhibit at the I.P.M.A. Meetings. We invite members of the association to visit us. Specializing in medications for the treatment of arterial hypertension we will display several of our products of Potassium Thiocyanates including the newer products using Rutin in combinations. Other interesting pharmaceuticals will also be on display.

TAMPAX INCORPORATED
 New York, N.Y.
 Booth 226

Patients are constantly demanding authoritative information and up-to-date instruction in the use of the Tampax method of menstrual protection in three absorbencies. Tampax educational consultants will welcome the opportunity to discuss with you the many hygienic features of this leading intravaginal tampon.

THE TARBONIS COMPANY
 Cleveland, O.
 Booth 194

TARBONIS presents a unique tar extract 5 per cent (special process), in a clean patient-appreciated form, odorless, greasless, nonstaining. Its antipruritic, decongestant, remedial properties are of established value in every form of eczema, psoriasis, folliculitis, seborrheic dermatitis, industrial dermatoses, and in a number of other, especially pruritic disorders. SUL-TARBONIS (TARBONIS with 5 per cent sulfathiazole) provides a combination treatment (see indications above) when infection is a complicating factor.

THE TECHNICON COMPANY
 New York, N.Y.
 Booths 152-153

The Technicon exhibit will feature the use of both the AUTOTECHNICON for automatic processing of tissues for microscopic examination, and the scopicon, a device for the demonstration of microscopic pathology. Microscopic slides will actually be stained by means of AUTOTECHNICON during the course of the meeting. Also on exhibit will be the "Lab-aid" slide filing system, the Technicon Automatic Pipette Washer and the Technicon Constant Temperature Water Bath for spreading paraffin sections.

CHARLES C THOMAS
 Springfield, Ill.
 Booths 181-182

Charles C Thomas, Publisher's massive exhibit of books will be conveniently arranged for your browsing pleasure. These new titles will be featured: Klemme—*Hospital Care of Neurosurgical Patients*; Hepler—*Clinical Laboratory Diagnosis*; Myers and McKinlay—*The Chest and the Heart*; Overholt and Langer—*The Technique of Pulmonary Reconstruction*; and Padgett and Stephenson—*Plastic and Reconstructive Surgery*. A host of new monographs in the AMERICAN LECTURE SERIES will be on display.

U. S. STANDARD PRODUCTS CO.
 Woodworth, Wis.
 Booth 70

We invite you to visit our booth at the Interstate Post-graduate Medical convention in Cleveland. Sales and technical representatives should be in attendance to furnish you with information on our products.

U. S. VITAMIN CORPORATION
 New York, N.Y.
 Booth 116

Full color illustrated brochure "Diagnosing Vitamin Deficiencies" together with professional samples and literature on VI-SYNERAL, POLY-B, VI-LITRON, HYPERVITAM, LIPO-HEPLEX, DALSOI, DESIVER, AMIPROTE, RUTIN-ROUTASCOR, LIPO-ISCHEOL, TRI-SULFANYL and others.

THE UNIVERSITY OF CHICAGO PRESS
 Chicago, Ill.
 Booth 46

Distinguished for authoritative content and excellence of editorial work, the books of UNIVERSITY PRESSES claim enviable rank among nonfiction and technical publications. The Association of American University Presses has arranged a cooperative exhibit for your enjoyment at this meeting—and to give you an opportunity to purchase some of these important titles for your library.

THE UPJOHN COMPANY
 Kalamazoo, Mich.
 Booths 157-158-159

ADRENAL CORTEX AND RESISTANCE—The central panel of the exhibit symbolizes that man's resistance to stress is being increased by science. The other panels show the effect on the adrenals of various stresses—infection, exercise, surgery, and anoxia. The final panel shows the relative potency of adrenal cortex and lipo-adrenal cortex sterile solutions.

VAN PELT AND BROWN, INC.
 Richmond, Va.
 Booth 180

Of special interest is Vifoliron, the new and effective blood builder containing ferrous gluconate, ferrous sulfate, liver concentrate, folic acid, and supplementary vitamins. Barbidonna, sedative and spasmolytic preparation, is also being featured. This preparation is now available both in tablet and elixir forms. Inquiries are cordially invited concerning these and our other ethical pharmaceuticals.

VAPONEFRIN COMPANY
 Upper Darby, Pa.
 Booth 191

The Vaponefrin exhibit features devices and materials for use in Aerosol or Inhalational Therapy. This comprises the Vaponefrin Nebulizer and solution. The RSP unit (positive negative pressure) for sinusitis, the Vapocillin unit for the treatment of serious respiratory diseases of the chest and lungs and the new Vaponefrin Aerosol Motor Unit for production of low compression aerosols. Vaponefrin is an especially purified racemic epinephrine and is used alone as a bronchodilator or in combination with antibiotics for aerosol therapy.

VARICK PHARMACEUTICAL COMPANY, INC.
 New York, N.Y.
 Booths 31-32

Varick Pharmaceutical Company, manufacturers of DIGITALIS NATIVELLE, are proud to present an interesting and informative exhibit on heart disease. Featured will be DIGITALIS NATIVELLE, crystalline digitoxin, the chief cardioactive glycoside of digitalis purpurea. Physicians are cordially invited to listen via individual headsets to our stethoscopic reproductions of normal and abnormal heart sounds, and to view our presentation of enlarged full-color kodachromes of many gross cardiac specimens and photomicrographs of

cardiac pathology. Samples and literature of DIGITALINE NATIVELLE will be available.

WALLACE & TIERNAN PRODUCTS, INC.
Belleville, N. J.
Booth 176

Visiting physicians are cordially invited to visit the Wallace & Tiernan exhibit. In addition to the widely used prescription specialties—Azochloramid, Monomestrol, and Desenex—we will display Sotradecol, the new Council Accepted sclerosing agent for the injection treatment of varicose veins.

WILLIAM R. WARNER & COMPANY
New York, N. Y.
Booth 85

William R. Warner & Company will feature Heparin/Pitkin Menstruum, the latest in anticoagulant therapy. Other important preparations—Intracillin, a penicillin in oil without wax which exhibits prolonged and effective blood levels; Gelucillin "PR," a procaine penicillin; Diatrin, a new antihistaminic of extremely low toxicity, and other well-known Warner products will also be displayed.

WESTWOOD PHARMACAL CORPORATION
Buffalo, N. Y.
Booth 33

Presents WESTSAL, the newly developed and *only* salt substitute that tastes *exactly* like salt. Now possible to prescribe low-salt diets for cardiac, hypertensive and pregnancy toxemia patients without sacrificing palatability of meals. WESTSAL contains no sodium and can be used in cooking, baking and on the table without loss of flavor. There is no patient resistance to food seasoned with WESTSAL. Please stop at our booth for full particulars and a taste.

WHITE LABORATORIES, INC.
Newark, N. J.
Booth 1

White's Dienestrol Tablets and Dienestrol Suspension (Council Accepted)—a new orally effective synthetic estrogen is featured. Complete information and literature are available regarding the advantages of Dienestrol's high biologic activity, excellent patient-tolerance and economy. Other products of White Laboratories, Inc. are on display and White's Medical Service Representatives in attendance will be pleased to supply any further information requested.

WILLIAMS & WILKINS COMPANY
Baltimore, Md.
Booth 178

The Williams & Wilkins Company will exhibit about 30 new books and new editions which have been published in 1948. In addition, their complete group of medical periodicals will be displayed. This includes *Excerpta Medica*, the series of 15 abstract journals covering the world's medical literature classified according to subject matter.

WINTHROP-STEARN'S INC.
New York, N. Y.
Booths 93-94

Winthrop-Stearns Inc.—new owner of the businesses formerly conducted by Winthrop Chemical Co. and Frederick Stearns & Co.—features transparencies of beautiful medical art by Mr. Leon Schlossberg. This well-known artist was a pupil and associate of the late Max Broedel, the dean of medical artists and the first American professor of medical art (at Johns Hopkins University). His work reflects the impressive style of Broedel to which has been

added a unique transparency technic. Also featured will be the latest therapeutic contributions made by this firm.

MAX WOCHER & SON COMPANY
Cincinnati, O.
Booths 15-16-17

The firm of Wocher has a slogan that goes: "Your grandfather's instruments came from Wocher's." This 111-year-old firm has developed many new and interesting instruments for display at the I.P.M.A. meeting. In dealing with Wocher you have the opportunity of buying direct from the manufacturer of both instruments and a complete line of physicians' and hospital furniture. The Wocher organization, despite its century-old background, has a progressive and service-conscious attitude.

WYETH INCORPORATED
Philadelphia, Pa.
Booths 3-4

Wyeth Incorporated will feature Meonine[®] and Amphojel[®]. Meonine (dl-Methionine), the most efficient single agent for treatment of liver damage, is particularly effective in early portal cirrhosis and related conditions. Amphojel (Alumina Gel) is standard treatment for peptic ulcer. It is prepared in seven forms to meet individual needs. The Wyeth representatives in attendance will be glad to answer questions on these and other products. They will also have an ample supply of samples and literature.

YEAR BOOK PUBLISHERS, INC.
Chicago, Ill.
Booth 118

The Year Book Publishers are happy to present to the Assembly books written primarily for the man in practice who has finished his training but wishes to keep abreast of latest medical advancements. Recent Year Books, General Practice Manuals, Monographs and Texts will be shown; new and of especial interest will be *Methods in Medical Research*, Wright's *Vascular Diseases in Clinical Practice* and Young's *The Skull, Sinuses and Mastoids*, completing the Series of Roentgen Diagnosis.

F. E. YOUNG & CO.
Chicago, Ill.
Booth 196

F. E. Young & Company will exhibit Young's rectal dilators. These are a set of graduated sized dilators used in the treatment of constipation, hemorrhoids, rectal neurosis, etc. They are used by surgeons for postoperative anal contraction. The obstetrician and gynecologist find them a valuable aid in perineal repair. F. E. Young & Company will also display Sulf-A-Test, a ten second test for all sulfa drugs and Young's PSP Spot Test for kidney function study.

ZIMMER MANUFACTURING COMPANY
Warsaw, Ind.
Booth 221

Zimmer Manufacturing Company will exhibit a complete line of Fracture Equipment, including the latest developments in Bone Plating Instruments. New items on display for your approval will be: the BISHOP LOW SPEED OSCILLATING ATTACHMENTS FOR YOUR LUCK BONE SAW, A COMPLETE NEW SET OF MYERDING BONE CHISELS-GOUGES-OSTEOTOMES in one piece stainless steel, MOREIRA STUD-BOLT, ADJUSTABLE BONE CLAMPS, INTRAMEDULLARY PINS & INSTRUMENTS, THREADED WIRES & PINS, NEW TYPE SMITH-PETERSON NAIL & PLATE, RUBBER CUSHION WALKING HEELS, NEW WIRE & PIN CUTTER, STAPLE SET, and THE VINKE SKULL TRACTOR.

New Drugs and Instruments

Information published in this department has been supplied by the manufacturers of the products described.



HEARING AID BATTERY

PURPOSE: A new re-chargeable hearing aid battery.

DESCRIPTION: A wet-cell A battery offering up to eighteen hours of heavy service with one charge. The battery charges in six hours to full strength, using miniature charger plugged into regular AC outlet. It weighs only 5 ounces, is fully contained in a plastic case measuring $1\frac{1}{4}''$ by $\frac{7}{8}''$ by $3\frac{3}{4}''$, and fits any two unit hearing aid.

PRODUCER: Kenneth B. Butler & Associates, Mendota, Ill.

ENTEROGASTRONE

PURPOSE: For inhibiting gastric secretion and protecting the gastric and duodenal mucosa from ulceration.

COMPOSITION: A sterile lyophilized extract of the first six feet of intestine distal to the pylorus of freshly slaughtered hogs prepared according to the method of Ivy, *et al.*

DOSEAGE AND ADMINISTRATION: Best results have been obtained by the daily intramuscular injection of 200 mg. of enterogastrone dissolved in 4 or 5 cc. of solvent. Injections should be continued for a period of at least one year.

CAUTION: The preparation is not entirely free from vaso-depressor effect, and if given intravenously will produce weakness and flushing of the face.

HOW SUPPLIED: Enterogastrone Hydrochloride (Armour) is supplied in a 10 cc. size rubber stoppered vial containing 200 mg. of lyophilized enterogastrone, together with a 5 cc. ampule solvent.

PRODUCER: The Armour Laboratories, Chicago 9, Ill.

PRENATAL CAPSULES LEDERLE

PURPOSE: To supplement the diet with vitamins and minerals during pregnancy and lactation.

COMPOSITION: Each capsule contains

Vitamin A	600 U.S.P. units
Vitamin D	200 U.S.P. units
Thiamine hydrochloride (B_1)	2 mg.
Riboflavin (B_2)	5 mg.
Ascorbic acid (C)	5 mg.
Nicotinamide	7 mg.
FOLVITE* folic acid	1 mg.
Calcium (in CaHPO_4)	250 mg.
Phosphorus (in CaHPO_4)	190 mg.
Iron (in exsiccated FeSO_4)	6 mg.
Manganese (in MnSO_4)	0.12 mg.

*Reg. U.S. Pat. Office.

DOSEAGE AND ADMINISTRATION: Three Prenatal Capsules Lederle daily supply the following percentages of adult minimum daily requirements: vitamin A 150 per cent, vitamin D 300 per cent, thiamine HCl (B_1) 600 per cent, riboflavin (B_2) 300 per cent, ascorbic acid (C) 350 per cent, calcium 100 per cent, phosphorus 76 per cent, and iron 180 per cent. In pregnancy and lactation, 50 per cent of the calcium and 38 per cent of the phosphorus minimum daily requirements are supplied by three capsules daily.

HOW SUPPLIED: Packages of 100 capsules.

PRODUCER: Lederle Laboratories Division, American Cyanamid Company, Pearl River, N.Y.

PENICILLIN CALCIUM TABLETS

PURPOSE: Treatment of pneumococic, streptococic, staphylococic, and gonococic infections.

COMPOSITION: Each tablet contains 100,000 units of the calcium salt of penicillin, buffered with 0.3 gm. of sodium citrate.

CAUTIONS: In syphilis, meningitis, endocarditis, and peritonitis, penicillin should be administered parenterally. In acute septicemia and bacteremia, parenteral administration of penicillin should be continued until negative blood cultures are obtained.

DOSEAGE AND ADMINISTRATION: Gonorrhea: 1 tablet every three hours for 6 doses per day for one to two days. In acute pneumococic, streptococic, and staphylococic infections, a minimum of 20,000 to 40,000 units of penicillin should be given parenterally every three hours. After the acute phase has been controlled, the treatment may be continued with one Penicillin Calcium Tablet every three hours for at least forty-eight hours after the temperature has returned to normal.

HOW SUPPLIED: In boxes of 12 tablets, each tablet individually hermetically sealed in metal foil. Penicillin Calcium Tablets do not require refrigeration.

PRODUCER: Schering Corporation, Bloomfield, N.J.

Leaves from a Doctor's Diary

By MAURICE CHIDECKEL

September 1 . . . It was a night to be remembered, as if a host of enigmas conspired to deprive me of my needed rest. 1:30 A.M. The psychic hiccuping of actress Jeanette disturbed the neighborhood. Between attacks she informed me of the cause of her unhappiness. The manager threatens to take her role away, because she does not put enough life in her death scene. 2:30 A.M. Mrs. Dougherty was seized with hysterical convulsions. Her brother, so her husband told me, is to be tried in criminal court for robbery of a bank. "They cannot put him in jail," she screamed. "That poor boy could not have done it. I am asking you, how could he have robbed a bank in Baltimore at twelve noon, when at that very hour he was robbing a bank in Washington?"



4:00 A.M. A full fledged case of hysteria in Mrs. Colbert. Her husband assured her that he would leave her if she does not stop playing cards nightly. "And I'll miss him so," she spoke weepingly. 5:00 A.M. and all is still not well. Rooted in the obsession that his good wife is unfaithful, he chose that hour to seek advice on how to learn of her unfaithfulness or to be assured of her fidelity. He has an affair, comes home any hour and she does not seem to care where he has been. John Cullins, by the way, is not the only man who believes in a double standard of morality. The gander may; the goose must not. Then came the dawn, and the voice

of grocer Balgerman, who opens his store daily at 4 A.M. "You know what diarrhea is? Well, I got it. Terribly constipated. What's that? You want to sleep? You doctors certainly got it good. I wish I was a doctor."

* * *

September 2 . . . Dr. Martin Craven is not easy to depict; nor is the cast of his ideas easily grasped. To himself he is a person of infinite importance. Ten doctors, myself included, were invited to his house. It was no energetic dispute, for no one disputed. He alone talked. The prose he read from a paper was lusterless and imageless, and also senseless. Poetical Colleague Balder called his language a pale verbal landscape, desolate and foul smelling. Dr. Craven praised effusively all those who fight for socialized medicine. The overemphasized praise not only became heavy and monotonous, but nauseating. Then he began to condemn all opponents.

What a relief when his wife came in. We all rose and went to the door. She seemed to be drenched to the bone. "It's raining hard," she said, without looking at any one of us. Dr. Craven glanced through the window and remarked: "A regular deluge." She asked: "A what?" He answered: "A deluge. Don't you know what that is? Didn't you read about Noah and the Ark and the animals he gathered. . . ." She interrupted angrily: "You know that I didn't have a chance to read a paper for a week. How do you expect me to know what's going on in the world?" As they began to argue, we sneaked out one by one, and so ended the important gathering to save humanity.

September 3 . . . Dr. Brace, too, never lacks a solution for the constantly recurring problems, and he too is not niggardly in the matter of faults. Once an idea dawns upon him, it gains unforced momentum, stiffens his will and the determination becomes unalterable. But the astute jobs he undertakes are never done and all his efforts end in nothing at all. In a few weeks there will be a scientific meeting, and we shall be honored by out of town medicos. We must have, the doctor says, an endless variety of clinical material for demonstration.

To each member of the clinic he assigned the task of getting the stuff. To me was assigned (I am quoting): "Six cases of breast malignancy that were benefited by testosterone, be it propionate, acetate, crystalline pellets, or methyl. Each patient to be allowed to tell her story. At least three cases of dysmenorrhea due to sexual suppression, that were cured by having the suppressed libido restored. Here, too, the girls must open up and tell all to those assembled.

"We must, we absolutely must, have a skin grafting demonstration, and we must prove that prepuces after circumcision make excellent grafts. Hence you are to bring nine fresh prepuces just cut off. We need six small ones and three from adults. You must not fail. Oh, yes, bring a badly burned case that needs grafting. No less than eight cases of migraine that shall furnish incontestable evidence of tension. We are to claim that migraine is a tension phenomenon. Tension, understand? Cerebral, vascular, sexual, as in my wife, and otherwise, but tension.

"Six cases of diffuse goiter and hyperthyroidism that were benefited by my favorite single therapeutic agent, radioactive iodine. For the sexologists bring two cases to show them that skipped menstrual periods increase sexual desire." End quote. I always thought that increased sexual desire is what



Treatment of Fistula-In-Ano

WITH SPECIAL REFERENCE TO ANO-RECTAL FISTULA

C. NAUNTON MORGAN*

LONDON, ENGLAND

IN ENGLAND, John Arderne wrote a treatise on fistula-in-ano as long ago as the fourteenth century and yet today, cure of an extensive fistula-in-ano is still a problem. We at St. Mark's Hospital have made a special study of some of these problems.

A fistula-in-ano results from nature's failure to obliterate an abscess cavity which arises in relation to the ano-rectal region. Imperfect healing by third intention, namely cohesion of granulation tissue allows the formation of the main track of a fistula. The principle of surgical treatment is the formation of a wound which will heal by second intention (healing from the base). This is done by laying open the main track and its offshoots, removing skin, etc., in order to fashion a flat wound.

Because the main track must be laid open from its internal to external openings, the problem arises of what portion of the ano-rectal musculature will require division.

Three important facts must be known in order to treat successfully a fistula-in-ano; firstly, the anatomy of the muscles; secondly, their

function and thirdly, the position of the main track in relation to the muscles.

The circular muscle coat of the rectum extends into the anal canal where it becomes enlarged to form the internal sphincter. It surrounds the anal canal and ends at a point just above the anal orifice. (Figure 1.) This sphincter, which is probably important in maintaining postural tone, has been mistaken in the past for the ano-rectal ring which it will be seen lies at the ano-rectal junction (*vide infra*).

External to the circular muscle is the longitudinal muscle coat. The longitudinal muscle of the rectum fuses with the puborectalis which is a part of the levator ani, to form the composite longitudinal muscle of the anal canal. This fibromuscular structure is inserted into the anal skin just within the anal orifice as the anal intermuscular septum and forms an important landmark, the *anal intermuscular depression*. (Figure 1.) An additional septum from the longitudinal muscle extends outwards between the subcutaneous external sphincter and the other parts of this sphincter across the ischio-rectal fossa to the ischial tuberosity. The ischio-rectal fossa is thus divided into the subcutaneous perianal space and the ischio-rectal space. The perianal space contains the subcutaneous external sphincter and the majority

*Surgeon to St. Bartholomew's Hospital; Surgeon to St. Mark's Hospital for Diseases of the Rectum; Surgeon to the Hospital for Tropical Diseases, etc., London, England.

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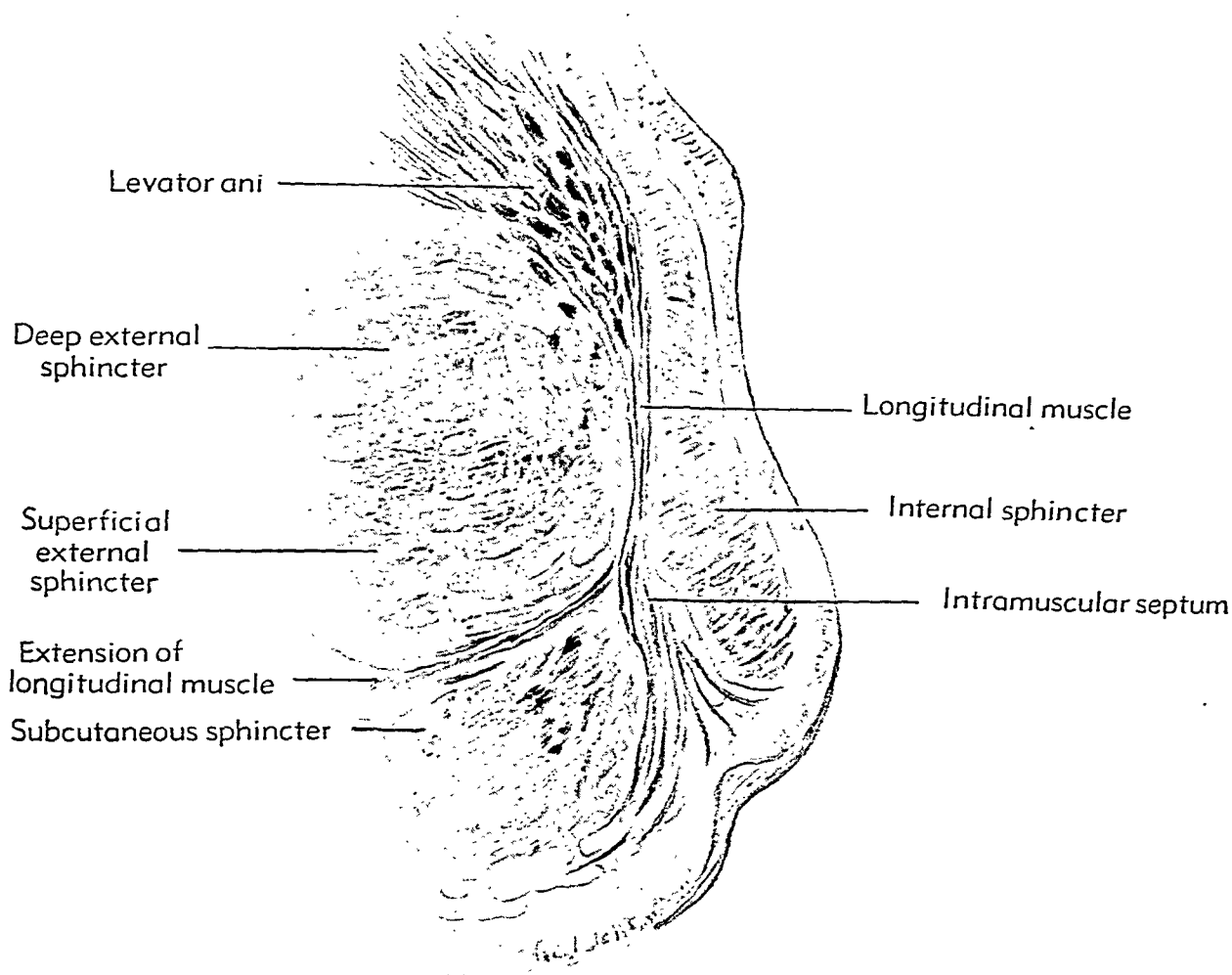


Figure 1. Sagittal section through ano-rectal musculature.

of fistulae lie within it. (Figure 11.)

The external sphincter muscle consists of three parts: subcutaneous, superficial, and deep. The two latter portions of the muscle surround the anal canal and lie external to the composite longitudinal muscle; the adjacent fibers of the deep external sphincter intermingling with those of the pubo-rectalis portion of the levator ani. The subcutaneous portion of the external sphincter is the only muscle surrounding the actual anal orifice. (Figures 1 and 2.)

The anterior and inferior fibers of the pubo-coccygeus portion of the levator ani which arise from the back of the pubis, form the strong

pubo-rectalis muscle. These muscle fibers pass backwards from the pubis on either side of the prostate or vagina to form a continuous sling of muscles behind the rectum. (Figure 3.) The muscular sling is in intimate contact with the lateral and posterior aspects of the ano-rectal junction; the gap left in the muscle ring anteriorly, at this level, being completed in front by the deep portion of the external sphincter. (Figure 2.)

The muscle ring thus formed by the pubo-rectalis sling and anteriorly by the deep external sphincter is called the *ano-rectal ring*—an important landmark in rectal surgery.

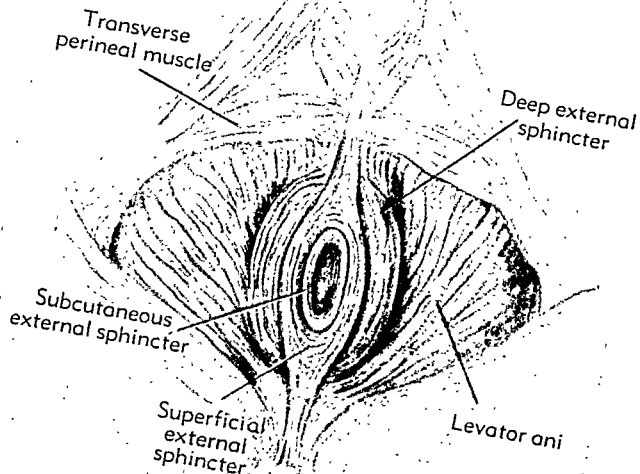


Figure 2. Ano-rectal musculature (from below).

It is the role of the puborectalis sling and the deep and superficial external sphincters to maintain continence. The subcutaneous external sphincter is of little importance in this respect and its function is probably that of preventing entrance into the rectum from without.

As long as a portion of the ano-rectal ring is preserved, good control of normal feces will be retained. It will be realized therefore that accurate location of the ano-rectal ring is of great surgical importance.

LANDMARKS

The ano-rectal ring can be felt when the finger is slowly withdrawn from the rectal ampulla into the anal canal and is also visible

through a proctoscope. (Figures 4 and 5.) The anal intermuscular depression formed by the insertion of the longitudinal muscle is also palpable and may be seen on a prolapsed hemorrhoid. Its position marks the upper limit of the subcutaneous external sphincter. (Figure 6.)

CLASSIFICATION OF FISTULAE

The most practical classification of fistulae is based on the relation of the main track to these palpable landmarks.

1. Subcutaneous and submucous (5 per cent) (no relation of surgical importance to muscle). (Figure 7.)
2. *Anal fistula*—Main track is situated below the ano-rectal ring but lies at or above anal

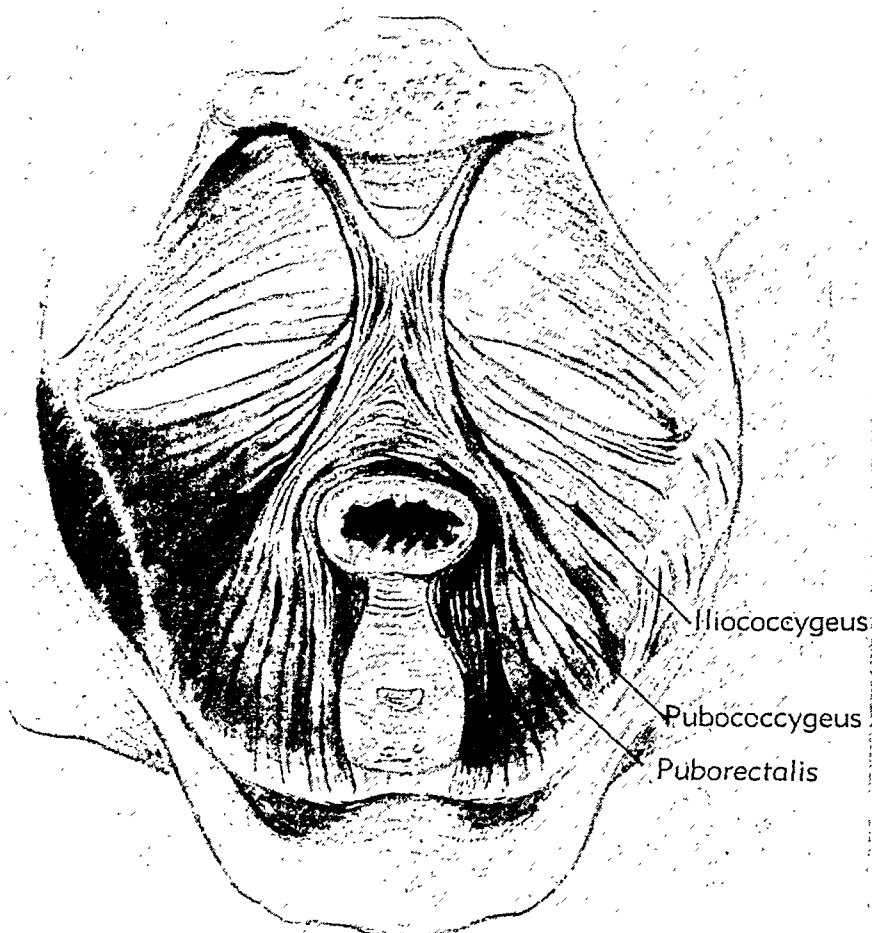
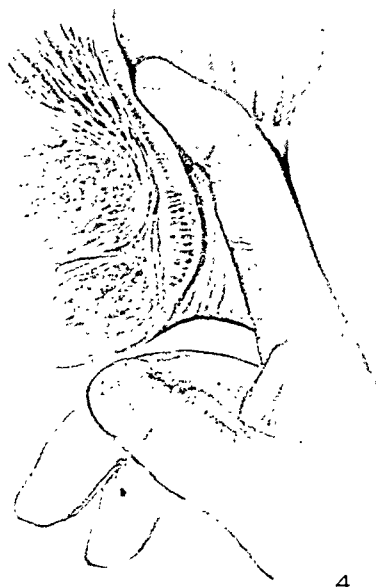
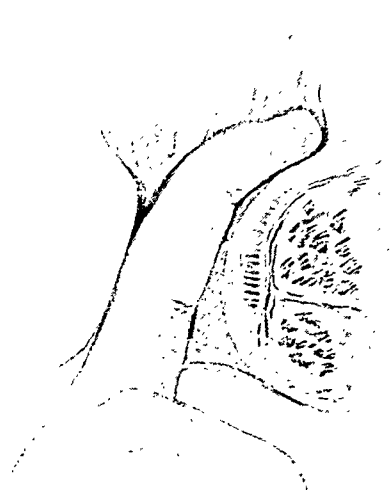


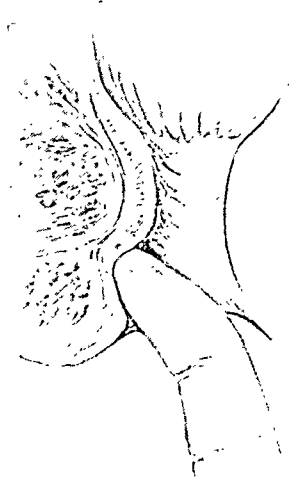
Figure 3. The levator ani muscles (from above).



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5



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Figure 4. Palpation of ano-rectal ring (labially and posteriorly). Figure 5. Palpation of ano-rectal ring (mid-line anteriorly where it is formed by deep portion of external sphincter only). Figure 6. Palpation of anal intra-muscular depression.

intermuscular depression (i.e., above subcutaneous external sphincter).

Low anal—At level of anal intermuscular septum (75 per cent).

High anal—Above the anal intermuscular septum but below the ano-rectal ring (15 per cent). (Figure 7.)

3. *Ano-rectal fistula*—Main track lies above level of the ano-rectal ring (5 per cent).

Full discussion of the diagnosis and treatment of all types of fistulae is not feasible here but it is pointed out that the main track of an anal fistula can be palpated under the skin running *radially* towards the anal canal and further, an inserted probe will also be found to lie in this direction. (Figures 8 and 9.) It is possible to lay open the main track completely and to fashion a flat wound because the main track lies below the ano-rectal ring. (Figure 10.)

It is the ano-rectal fistula which is the real surgical problem. The main track extends deeply into the ischio-rectal space above the level of the ano-rectal ring. It cannot be treated in the same manner as the foregoing types, since the ano-rectal ring lying on its inner wall, would be divided, resulting in incontinence.

ANO-RECTAL fistula arises from infection which has extended deeply into the ischio-rectal space. This space is bounded externally by the bony pelvis and obturator muscle and fascia, while its inner wall is formed by the inferior aspect of the levator ani and the ano-rectal musculature. (Figure 11.) The space extends upwards to the origin of the levator ani and passes under and above the transverse perineal muscle and triangular ligament. The pattern of this type of fistula is shaped by the position and form of the pubococcygeus and more especially the pubo-rectalis muscles. (Figure 12.)

The main track passes upwards in the ischio-rectal space, *parallel* to the anal canal and can neither be felt under the skin nor by the finger in the anal canal. (Compare radial probe of anal fistula.) (Figures 8 and 9.) It extends to the outer aspect of the puborectalis and inflammation may spread among the fibers of this

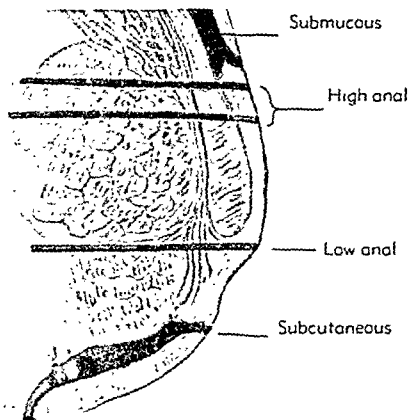
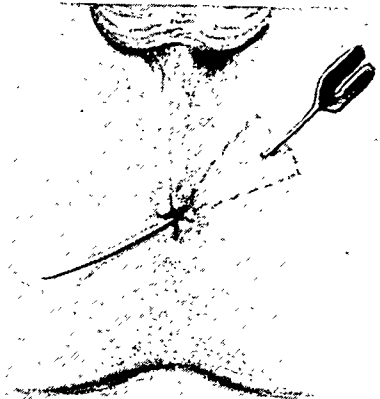
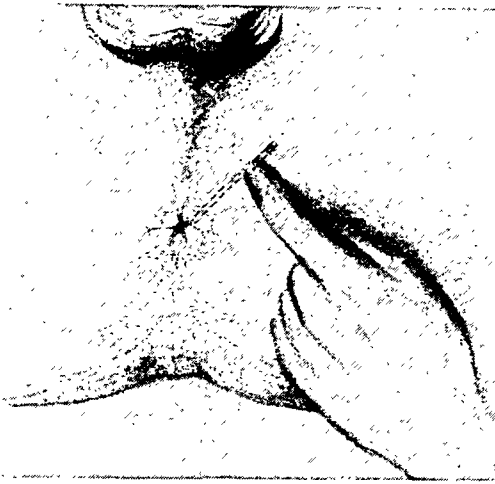


Figure 7. Closeup view of anal fistula.

muscle. In the rectum an induration is palpated just above the ano-rectal ring and the point of the probe can be felt in relation to this induration. When the uppermost limit of the parallel main track is reached, an anterior extension will be found running forwards along the puborectalis towards the pubis. Another extension to the opposite ischio-rectal space, running behind the ano-rectal junction along the sling fibers of this muscle and passing under the coccygeal origin of the superficial external sphincter, may be present. (Figure 13.)

Finally, an extension into the anal canal should be sought for with the probe and by palpation. The anterior extension and that to the opposite side lie on, or even in, the puborectalis and are in close relation to the bowel wall and therefore give the impression that the submucous coat of the bowel is involved. This is not the case, however, since if there be infection in the submucous layer, it would extend downwards and be felt below the level of the



Figures 8a and b. Low anal and subcutaneous fistulas may be palpated beneath the skin.

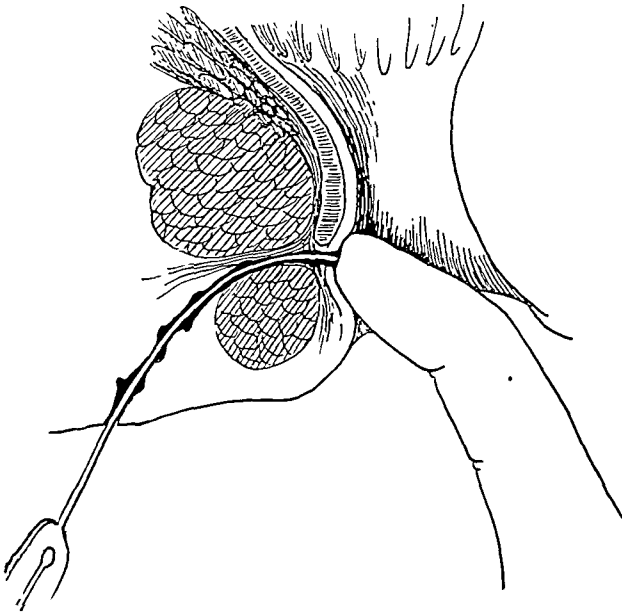


Figure 9. Anal fistula (low). Finger palpating radially or transversely; probe may be inserted through track.

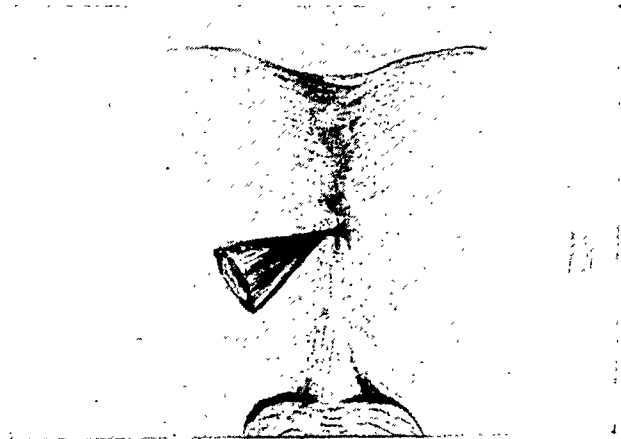


Figure 10. Track opened and skin removed to form a flat wound extending into anal canal.

ano-rectal ring in the anal canal. (Figure 14.)

If the induration which is palpable just above the ano-rectal ring in the case of an ano-rectal

fistula be mistaken for a submucous abscess and an incision made into it from the lumen of the bowel, an internal opening will be produced above the level of the ano-rectal ring. This is a disastrous mistake since such a fistula is usually incurable.

The internal opening in an ano-rectal fistula lies below the level of the ano-rectal ring. (Figure 15.)

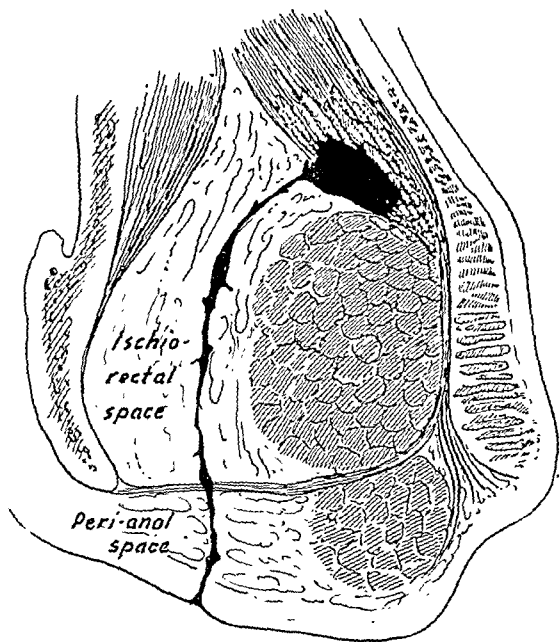


Figure 11. The ischio-rectal and perianal spaces.

TREATMENT

Patience, especially on the part of the patient, is necessary and the surgeon must have the pattern of this type of fistula clearly in his mind and be on the lookout, during the period of healing, for bridging of granulation tissue or for an overlooked extension.

Because the parallel probe lying in the main track extends deeply with its point in close proximity to the bowel wall, a guarding finger must be placed in the rectum while incision of the tracks is carried out. First, a deep incision is made along the probe in the main track directly backwards towards the coccyx cutting through skin and fat of the ischio-rectal space. When the sides of the wound are retracted, the

granulation tissue lying on the under surface of the puborectalis is seen. The anterior or forward extension is located and laid open in a forward direction, the transverse perineal muscle being divided.

Next the track to the opposite side is sought and opened. If this latter extension is present, repetition of the pattern may be found in the opposite ischio-rectal space. (Figure 12.)

The extension into the anal canal is finally looked for and the large cavity laid open into the anal canal.

Wide excision of skin and fat is necessary in order to make the large wound as shallow as possible, but in spite of this, the anterior part of the wound lying along and under the pubic

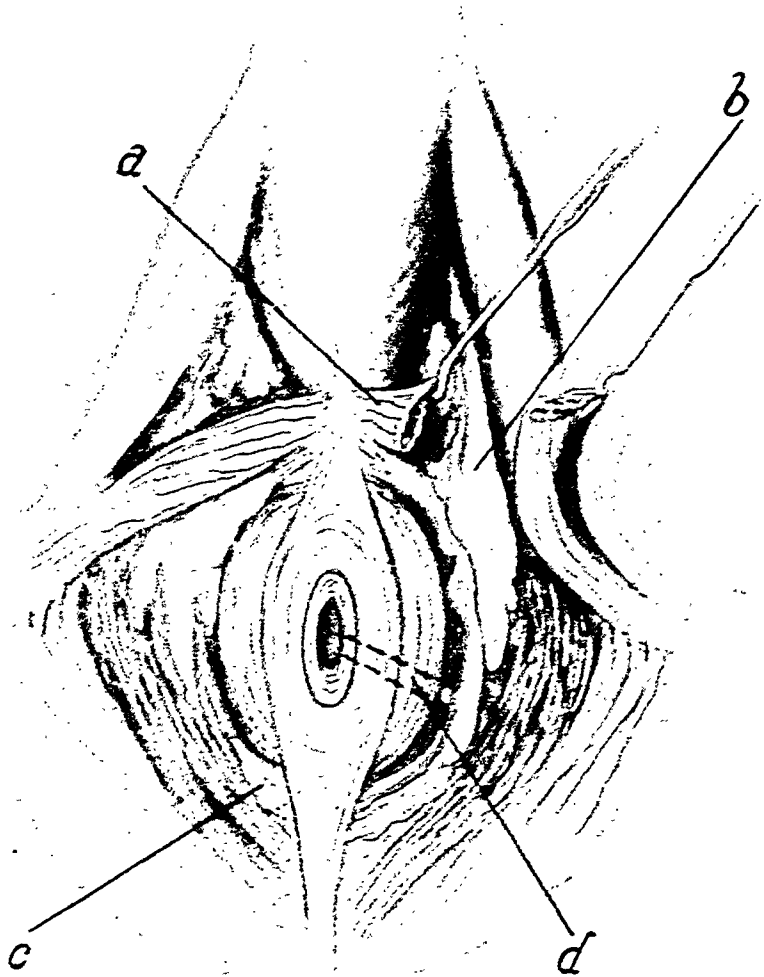


Figure 12. The pattern of an ano-rectal fistula (involvement of both ischio-rectal spaces). *a*. Transverse perineal muscle dissected. *b*. Forward or anterior extension. *c*. Extension to opposite side under coccygeal attachment of superficial portion of external sphincter. *d*. Extension into anal canal.

arch must remain as a deep cleft and bridging of granulation tissue across the healing wound must be prevented. Even if an extension into the anal canal is not found, division of the subcutaneous portion of the external sphincter together with the removal of skin at the anal verge should be carried out in order to flatten the wound at its inner aspect.

Flat dressings are placed in the wound in such a manner as to encourage healing by second intention.

The first redressing is done under pentothal anesthesia on the fifth day and then for the next week on alternate days. Any bridging of granulation tissue is broken down with the finger. Dressings and baths are then carried out twice daily. Several anesthetics may be required during the first few weeks in order to be sure that satisfactory healing is taking place.

In conclusion, we believe that the large majority of high anal fistulae are of the ano-rectal type and do not extend above the level of the

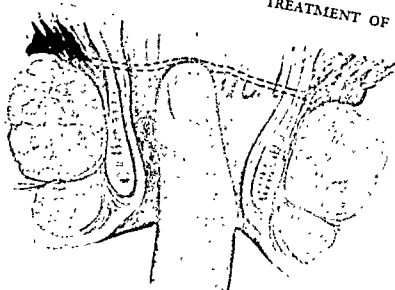


Figure 13. Extension to opposite side palpable through bowel wall.

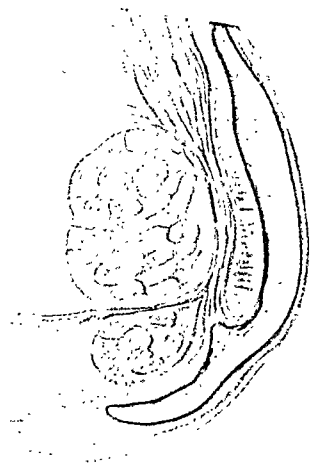


Figure 14. Extension of a submucous abscess downward in anal canal.

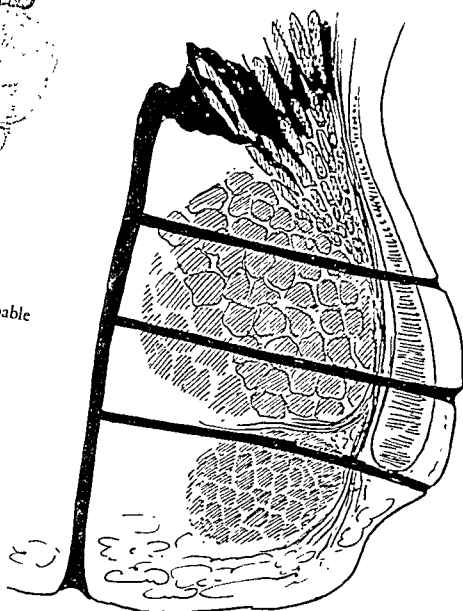


Figure 15. Possible levels of extension of ano-rectal fistula into anal canal.

levator ani muscle. A pelvesrectal or supralevator fistula or abscess is, in our experience, a great rarity.

If the anatomy of the puborectalis and the pattern of these fistulae are remembered, cure will be obtained, and in the words of William Shakespeare, the patient will not "persecute time with hope, finding no other advantage in the process but only the losing of hope with time," even though the wound may take several months or longer to heal.

REFERENCES

1. MILLIGAN, E. T. C., and MORGAN, C. NAUGHTON. *The Lancet*, 1934, Vol. 11, pp. 1150 and 1214.
2. GORDON-WATSON, SIR CHARLES: Collected papers of St. Mark's Hospital, London. Centenary Volume, p. 397.



Surgical Treatment of Coarctation of the Aorta

O. T. CLAGETT*

MAYO CLINIC, ROCHESTER

COARCTATION of the aorta was first described by Morgagni in 1760. Since that time numerous reports of single cases and occasionally more extensive reviews of the subject have appeared in the literature. For the most part, this literature has been concerned largely with the pathologic aspects of the problem. The first report on the possibility of a surgical attack on coarctation of the aorta was presented by Blalock and Park¹ in 1944. This work was confined to animal experiments. In the fall of 1944 Crafoord and Nylin² performed the first operation for this condition and in 1945 Gross and Hufnagel³ reported the cases in which they had performed operations as well as the extensive experimental work they had done preparatory to the development of techniques for this surgical procedure.

The developments in vascular surgery which now permit a surgical attack on coarctation of the aorta impose the responsibility of diagnosis of this condition on physicians everywhere. Coarctation of the aorta is no longer a subject of academic interest only. It is a matter of concern that this condition be diagnosed accurately

ly and that the diagnosis be established as early as possible so that operation can be performed before extensive vascular damage or cardiac failure develops to deny patients their chance to get well.

The common opinion that coarctation is so rare that it does not warrant consideration is not tenable. Blackford⁴ reported that coarctation occurs in one of every 1,500 of the population. Evans⁵ found 11 instances of the adult type of coarctation in 16,215 necropsies, or one in 1,474. Levine⁶ has estimated that 0.1 per cent of all persons have coarctation of the aorta. Lindgren⁷ found 3 instances in 10,000 necropsies. According to Abbott,⁸ of 1,000 congenital heart lesions, 176 were coarctation of the aorta. If one accepts only the more conservative estimates as to the incidence of this condition, it would still seem likely that in the United States there are at least 36,000 persons with this condition. It becomes apparent that the diagnosis of coarctation of the aorta is a matter of concern.

It is a peculiar paradox that although the diagnosis of coarctation of the aorta is not particularly difficult, it is rarely made. Abbott reported that in a series of 200 cases the diagnosis had been made clinically in only 4 per cent. In 1926 King⁹ reported that in the years 1889 to

*Division of Surgery, Mayo Clinic, Rochester, Minnesota.

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1923 at Johns Hopkins Hospital the diagnosis of coarctation of the aorta was made in only one instance. In the group of cases in which I have performed operations, one-half have been referred to the clinic for sympathectomy for hypertension. Apparently coarctation had not been considered as a possibility.

Coarctation of the aorta occurs in males three times as frequently as in females.¹⁰ It may be of the infantile or adult type. In 176 cases reported by Abbott, the lesion was of the adult type in 105 and of the infantile type in 71. Bonnet¹¹ has offered a classification that is helpful in distinguishing the two varieties (Table 1).

The infantile variety is not of great concern from a surgical standpoint since lesions of this type, for the most part, are not amenable to surgical treatment owing to the frequent association of other anomalies that are not compatible with life. According to Abbott, other anomalies are present in 40 per cent of cases of coarctation. The most common associated anomaly in the adult type of coarctation is bicuspid aortic valves.¹²

The degree of coarctation may vary considerably from only slight narrowing of the aorta to complete stricture. In 200 cases Abbott found complete stenosis in 47, extreme stenosis (to 0.6 mm.) in 108 cases, and moderate stenosis (caliber one-third of normal) in 45 cases. The strictured site may be very short or several centimeters long.

COARCTATION of the aorta is compatible with a long and fairly normal life in rare instances. One patient has been reported to have lived 92 years.¹³ However, the prognosis of this disease is extremely poor in most cases. According to Abbott, 74 per cent of the patients die before the fortieth year of life and the average age at death is only 32 years. In general, death from this condition can come about in one of three ways. Death of a person in apparently good condition may occur suddenly from rupture of the aorta or of a cerebral aneurysm. Sudden cardiac failure may develop in a young,



O. THERON CLAGETT

apparently normal person, or there may be evidence of a progressive vascular disease with dyspnea, fatigue, legache, headache, dizziness, sense of fullness in the head, buzzing in the ears, flushed face, epistaxis, and gradual heart failure.

In a group of cases reported by Abbott, death was due to cardiac decompensation in 60, to rupture of the aorta in 44, to rupture of a cerebral vessel in 24, and to bacterial endocarditis in 10. In Blackford's 196 cases, 68 patients died of gradual heart failure, 16 of sudden heart failure, 38 of ruptured aorta, 25 of cerebral hemorrhage, and 6 of bacterial endocarditis. These figures serve to indicate the course of events in most cases of coarctation and emphasize the importance of establishing the diagnosis before cardiac failure or extensive vascular changes develop that will prevent consideration of surgical intervention.

Coarctation of the aorta of the adult variety rarely causes any symptoms or signs that call attention to its presence during the early years

TABLE I
DISTINGUISHING FEATURES OF INFANTILE AND ADULT TYPES OF COARCTATION OF THE AORTA (AFTER BONNET¹¹)

DISTINGUISHING FEATURES	COARCTATION, TYPE	
	INFANTILE	ADULT
Site of coarctation.....	Above ductus	At or below ductus
Ductus arteriosus.....	Open	Closed
Associated anomalies.....	Frequent and major	Rare and minor
Collateral circulation.....	Absent	Present
Age.....	Newborn or infants	Children or adults

of life. In few persons under 18 to 20 years of age has the lesion been recognized. In many instances the first evidence of abnormality has been the detection of elevation of the blood pressure during a routine physical examination required for employment, insurance, school, or the armed services during the war. If clinical symptoms are present they are usually fatigue, headache, blurred vision, ringing in the ears, legache, bouts of dizziness, and pain in the back and shoulders. The important fact about coarctation that I wish to emphasize above all else is that the examination of any patient found to have an elevation of blood pressure in the arm must include an examination of the abdomen for pulsation of the abdominal aorta and of the legs for pulsation of the femoral and popliteal arteries. The occurrence of a weak or absent pulsation in these regions and of strong pulsation in the vessels of the head, neck, and upper extremities together with elevation of the blood pressure in the arm is strong evidence that coarctation is present.

Further evidence of coarctation is the presence of extensive collateral circulation from the upper to the lower part of the body. This is most marked in the region between the shoulder blades where large, pulsating vessels may be palpable. There may even be a palpable thrill and audible bruits in this region. I should like to urge that the examination of children in particular include check of the blood pressure and examination for pulsation in the lower extremities. This examination is frequently neglected since it is usually assumed that children do not have hypertension. The diagnosis of coarctation in children is particularly im-

portant since they are obviously the most favorable candidates for successful operation.

Röntgenographic evidence of coarctation includes particularly notching of the ribs. This feature has been noted in children only 5 years old. The notching is most marked in the ribs of the upper posterior part of the thorax. The aortic bulb may appear small or it may be absent. There may be some widening of the ascending aorta but this is not constant. Roentgenoscopy may reveal rather marked pulsation of the superior mediastinal shadow. There is usually some rounding and enlargement of the left ventricle.¹²

There are many other methods of diagnosis available, such as angiocardigraphy, tomography, accurate determination of the intra-arterial blood pressure in the upper and lower extremities, and so forth. These procedures are of value in the careful preoperative study and evaluation of the condition but they are not necessary for establishment of the diagnosis.

I should like to emphasize again that the important procedures in diagnosis of coarctation are (1) to take the blood pressure in the arm as a part of the examination of every patient regardless of his complaint or age, (2) to consider the possibility of coarctation of the aorta in every patient who has elevation of blood pressure, particularly if the patient is young, (3) to examine the abdomen and legs for decreased or absent arterial pulsation, (4) to examine the area between the shoulder blades for evidence of collateral circulation, and (5) to make a roentgenologic study for confirmatory evidence in those cases in which

TABLE 2
COLLATERAL CIRCULATION IN COARCTATION OF THE AORTA¹⁵

SCAPULAR AND CERVICAL ANASTOMOSIS	<ul style="list-style-type: none"> a. Suprascapular and transversalis colli (from thyroid axis) b. Posterior scapular and superficial cervical (from transversalis colli) c. Long thoracic and subscapular with its dorsalis scapulae branch (from axillary artery)
INTERNAL MAMMARY ANASTOMOSIS	<ul style="list-style-type: none"> a. Superior epigastric with deep epigastric branches of the external iliac b. Musculophrenic with phrenic branches of the thoracic and abdominal aorta c. Mediastinal branches with mediastinal branches of the thoracic aorta d. Anterior intercostal with terminal branches of the aortic intercostal
INTERCOSTAL ANASTOMOSIS	<ul style="list-style-type: none"> a. Terminal branches with intercostal branches of the internal mammary b. Lateral branches with subscapular and long thoracic branches of the axillary artery c. Dorsal branches with the posterior scapular d. The first with the second intercostal (arising from the subclavian by the superior intercostal) e. Each intercostal with the intercostal arteries above and below
THE SPINAL ANASTOMOSES	The vertebral artery arising from the first part of the subclavian artery reinforces the spinal arteries in which the blood flows downward to reach the spinal branches of the aortic intercostal arteries. These pass through the intervertebral foramina. Also, branches from the inferior thyroid pass through the intervertebral foramina in the neck to join the spinal arteries.

coarctation is suspected. The diagnosis is not difficult. It can be made by methods available to all physicians.

It should like to call attention particularly to the fact that what is believed to be hypertension of pregnancy may be due to coarctation of the aorta. While males are more frequently afflicted with coarctation than females, the condition can occur in either sex. Some 39 cases of coarctation in pregnant women have been reported in the literature. A considerable number of these patients have died during pregnancy or labor from cerebral hemorrhages, ruptured aorta, or heart failure. The treatment of choice in such a case should be cesarean section at the onset of labor. The danger of allowing a woman with coarctation to go through a hard labor is obvious.

In coarctation of the aorta there is a most remarkable example of the extent of development of collateral circulation that is possible in the human body. In this condition the circulation of the lower part of the thorax, abdomen, and lower extremities must be supplied from vessels that arise from the arch of the

aorta. An extensive study of this circulation has been made by Bramwell and Jones.¹⁵ The main channels which they have described are listed in Table 2.

Much of the collateral circulation is exposed and many dilated vessels must be clamped and ligated when the posterolateral thoracic incision necessary in the surgical treatment of these lesions is made. The incision itself is a rather major and time-consuming procedure on this account.

The surgical treatment of coarctation of the aorta is a new development and the technic of the procedure is not established definitely as yet. At present it is believed that the operation is best performed through a posterolateral approach, with resection of a long segment of the fifth rib and additional posterior segments of the fourth and sixth ribs if necessary. In the adult type of coarctation under consideration, the stricture usually involves the aorta just distal to the point at which the left subclavian artery branches from the aorta. The site of stricture is readily apparent. The marked dilatation and tortuosity of the intercostal and internal mammary arteries is at once evident. The aorta above the stricture and the left sub-

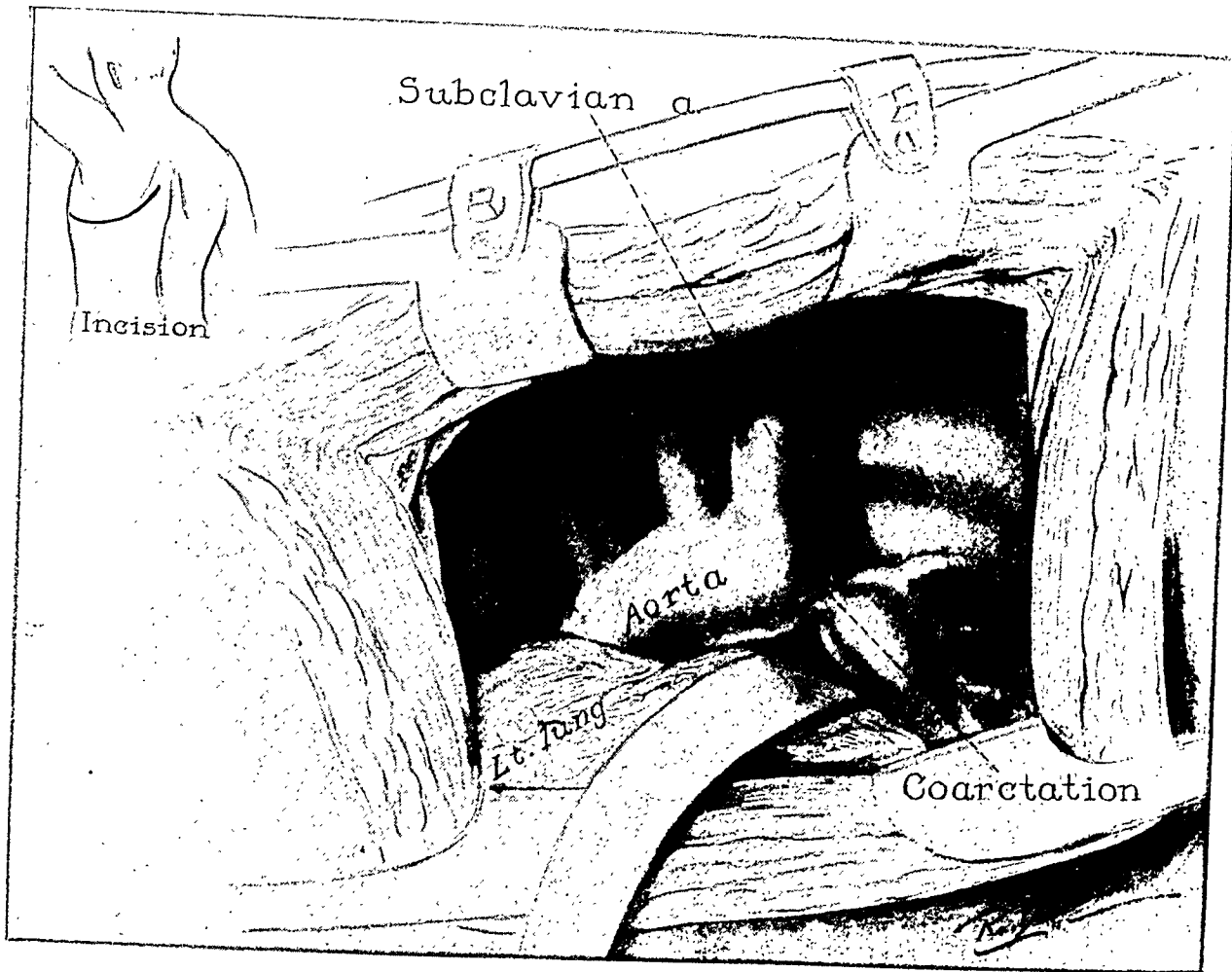


Figure 1. Exposure of coarctation of the aorta, showing enlarged intercostal vessels and stenosed area. The inset at upper left illustrates the operative incision.

clavian artery are larger than normal (Figure 1). The descending thoracic aorta is somewhat smaller than normal. The pleura over the aorta and subclavian artery is reflected and the mobilization of the aorta is initiated. This requires section and ligation of the first two pairs of intercostal arteries that come off the aorta distal to the stricture in most cases. These vessels are usually sclerotic and friable so that often this is one of the most difficult steps in the entire operation. There is usually a fibrotic band medial to the stricture that represents the obliterated ligamentum arteriosum. This must be severed.

AFTER the aorta has been mobilized above and below the stricture, a decision must be made as to whether it is feasible to resect the strictured part (Figure 2) and perform end-to-end anastomosis of the aorta (Figure 3) or whether the location or extent of the stricture requires section of the aorta distal to the stricture and use of the subclavian artery for anastomosis. Obviously the former is preferable, but when such is not possible, at the clinic we have been able to use the left subclavian artery to good advantage. When the subclavian is used the aorta is ligated at the site of a stricture, a clamp is placed across the aorta distally and the aorta

is sectioned. The left subclavian artery is then mobilized, the distal end is ligated as high as possible without interfering with the internal mammary artery, the proximal end of the subclavian artery is rotated, and end-to-end anastomosis with the thoracic aorta is performed (Figure 4). Usually these vessels are approximately the same size.

The anastomosis is carried out with the aid of fine silk sutures on atraumatic needles, and the edges of the vessels are everted by a continuous mattress suture technic that brings intima to intima with a minimum of suture exposed in the lumen of the vessel. Clamping of the aorta for the time necessary for performance of the anastomosis is not a problem since the collateral circulation previously established as a result of the lesion provides adequate blood supply to the lower part of the body.

At the clinic we have had no difficulty with the left arm in those cases in which the left subclavian artery was used for anastomosis. Collateral circulation has been adequate. The left arm becomes cooler than the right and pulsation may not be palpable for some weeks but there has been no significant weakness or dysfunction of the arm resulting from the procedure. When the anastomosis has been completed the vessel is occluded between the fingers, and the clamps, first below and then above the site of anastomosis, are removed. The occlusion of the vessel is released gradually,³ as advised by Gross, in order to avoid sudden heart failure from too rapid release of blood from the heart. In a few cases we have placed Gelfoam or oxidized cellulose around the site of anastomosis for additional protection against leakage. Pleura is then sutured over the site of anastomosis, the lung is inflated, and the thoracic wall is closed.

Immediately after opening the vessel at the site of anastomosis there has been a gratifying drop of blood pressure in the arm in most of our cases, and pulsation of the femoral vessels, which previously was absent, has become apparent. In a few of our cases the fall in blood pressure the first few days has not been remarkable but gradually the pressure has taper-



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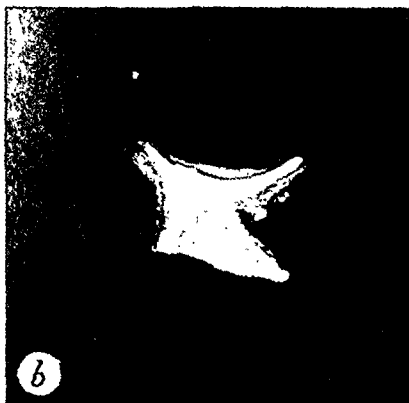


Figure 2a. Excised segment of the aorta; b, longitudinal section of excised portion of the aorta.

ed off toward normal levels during the period of hospitalization. Patients are kept in bed seven to ten days and are kept in the hospital two to three weeks.

OUR series of cases is not large. It consists of 14 operations. There were 9 males and 5 females in this group. Their ages varied from

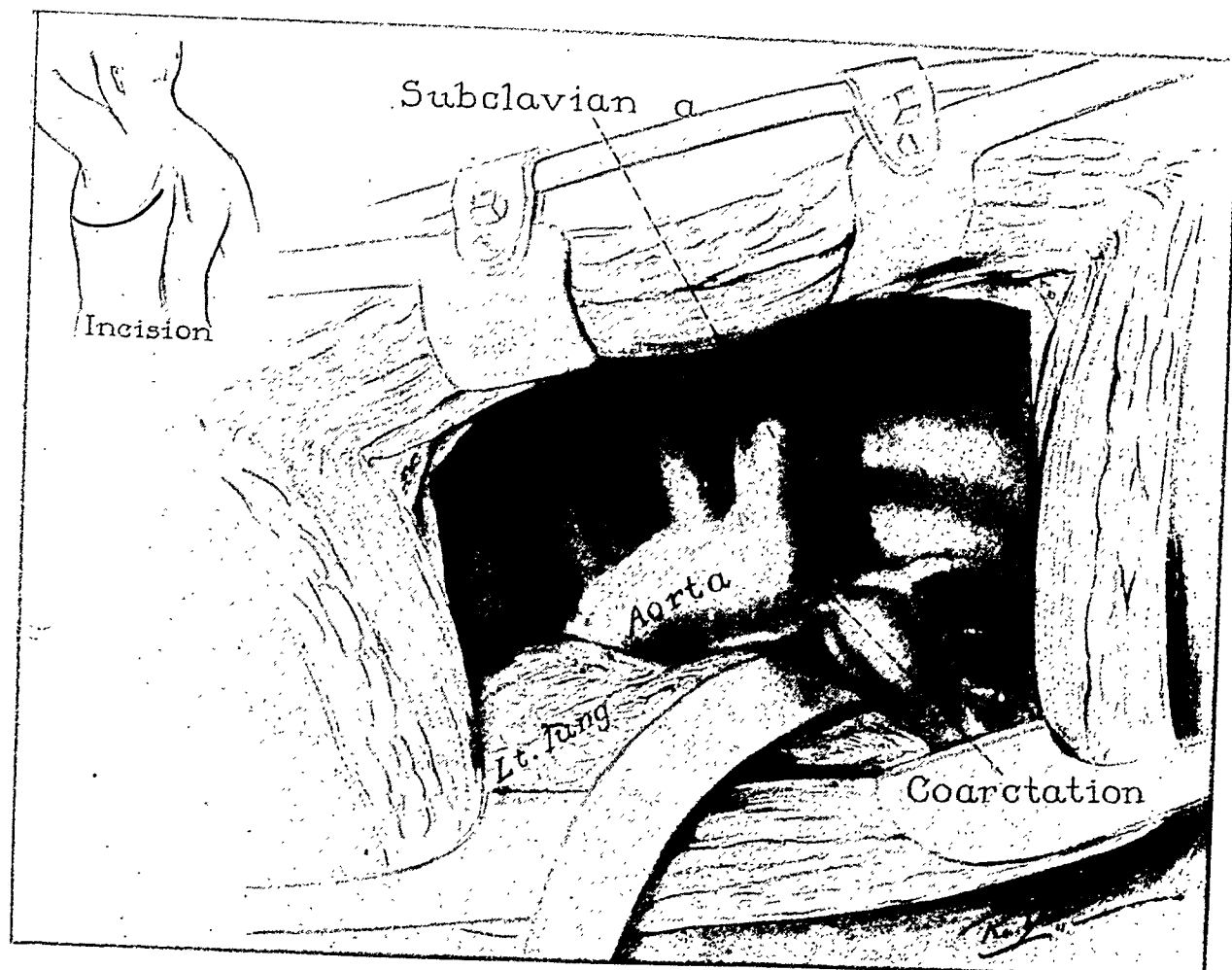


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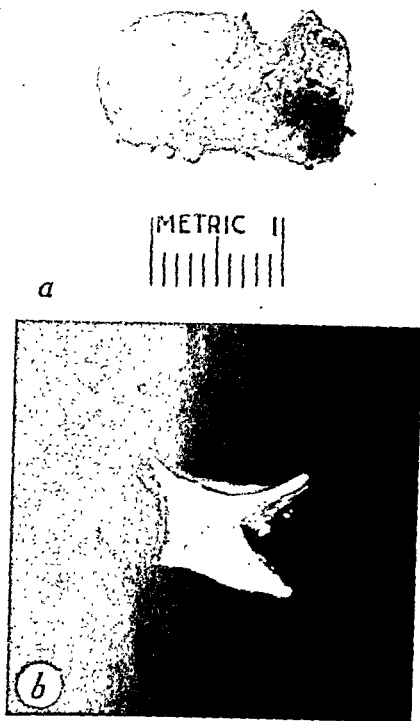


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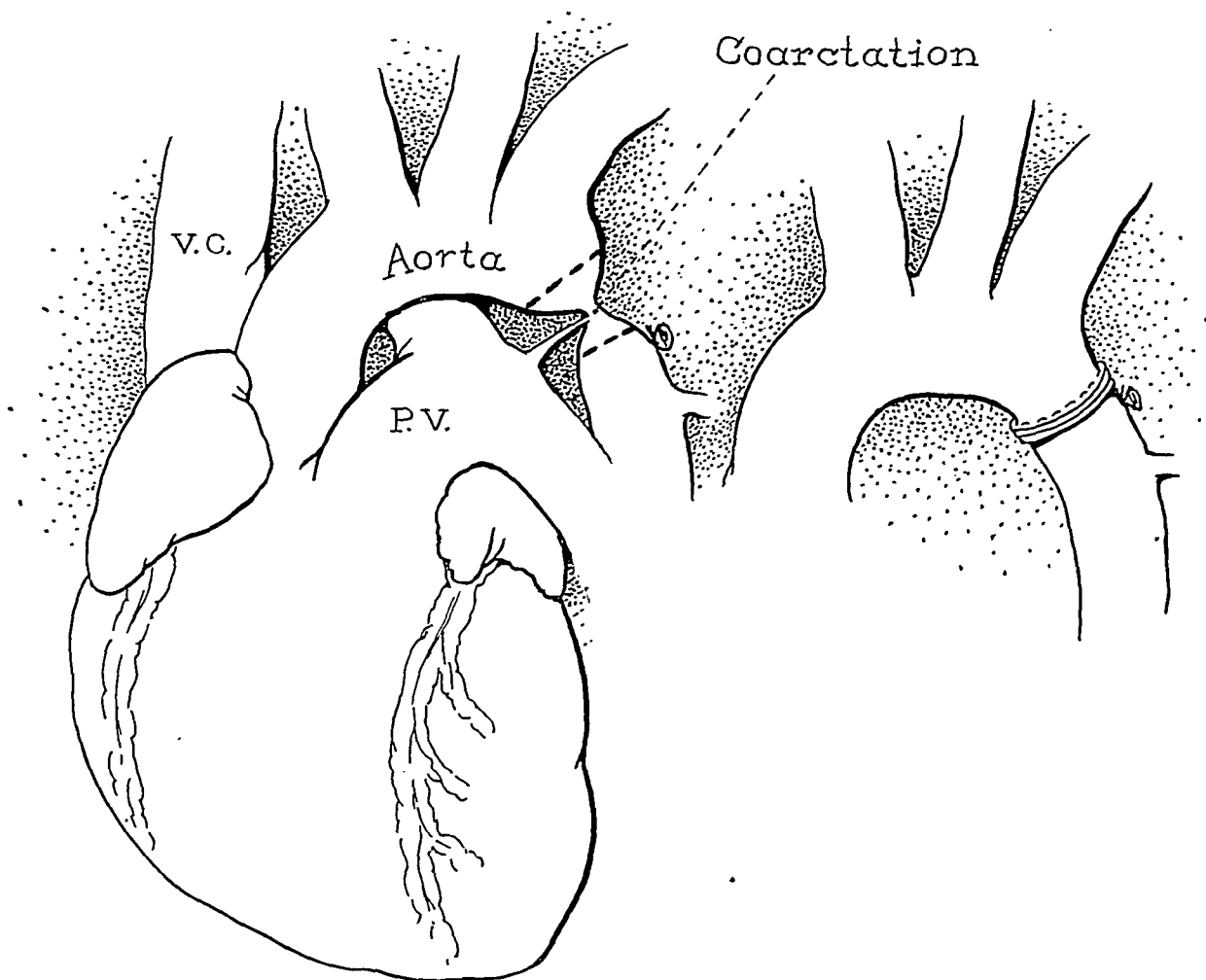


Figure 3. Left, diagrammatic representation of coarctation of the aorta; right, end-to-end anastomosis of the aorta.

11 to 34 years. In most of these cases there had been no symptoms which called attention to the abnormality until the patient had reached early adult life. The first indication in several was the finding of elevation of blood pressure during routine examination for employment, insurance, school, or the armed services during the war. In one case a diagnosis of hypertension of pregnancy was made when elevation of blood pressure was found during antepartum examination.

In half of the patients on whom we have performed operations at the clinic a diagnosis of essential hypertension had been made and

the patients had been referred for sympathectomy. The systolic blood pressure in the arm in our patients varied from 200 to 250, expressed in millimeters of mercury. The blood pressure in the legs was low or unobtainable; notching of the ribs and reduced or absent aortic knob were present in all cases. On close questioning, symptoms of coarctation described previously could be elicited in all cases. One patient had had one bout of cardiac decompensation and one had had two episodes suggesting a minor cerebrovascular accident. Several complained of fatigue, headache, dizziness, and so forth.

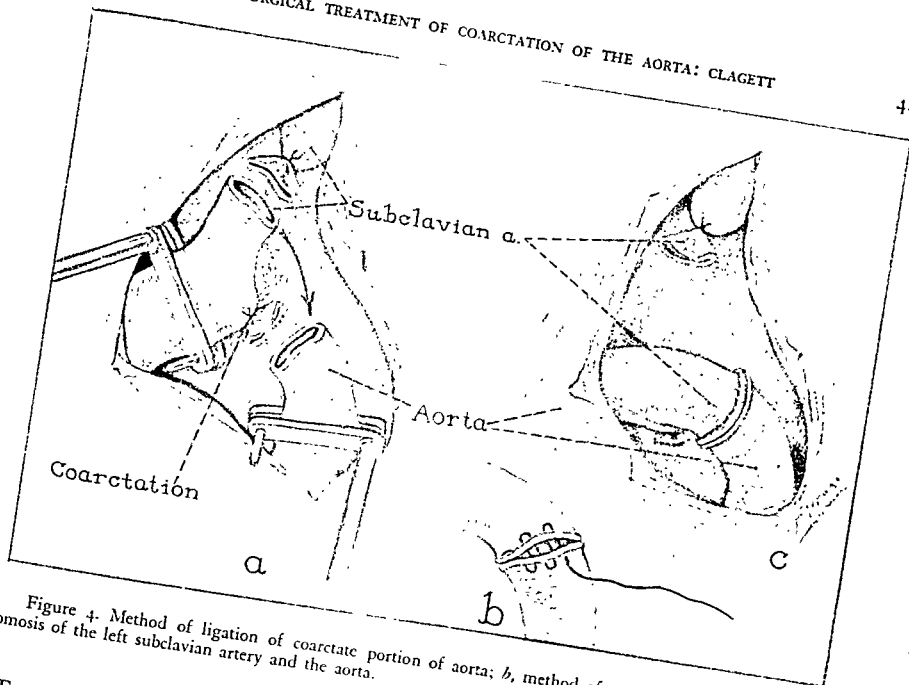


Figure 4. Method of ligation of coarctate portion of aorta; *b*, method of suturing; *c*, end-to-end anastomosis of the left subclavian artery and the aorta.

Four patients in our series died postoperatively. One had had cardiac failure previously and his death, two days after operation, was due to cardiac failure. The anastomosis at post-mortem examination was intact. The second death occurred thirty-two days after operation from hemorrhage due to separation at the site of anastomosis. The third death was due to a leak at the anastomosis eight days after operation. The fourth death was due to cardiac failure at the time of operation. Three patients have not obtained satisfactory decrease of the blood pressure in the upper part of the body although the blood pressure and the amplitude of the arterial pulsations in the lower extremities have been definitely increased. These patients had extensive sclerotic changes in their blood vessels and in each case there was a long stricture which necessitated use of the sub-

clavian artery. In each the thoracic aorta was much smaller than normal. Seven patients have gotten along very well and have been relieved of abnormal blood pressure and clinical symptoms. The results in these patients have been most encouraging.

IT SHOULD be emphasized that the surgical treatment of coarctation is now in an experimental phase. Not enough patients have been operated upon and followed over a time long enough to permit accurate evaluation of the results. It may be that the vascular changes resulting from prolonged hypertension may be so severe that these patients will suffer from these vascular changes in the future. There may still be danger of cerebrovascular accidents and so forth. If the diagnosis of coarcta-

tion can be established before extensive vascular changes have developed, the results from operation should be a great deal better. Therein lies the responsibility of the medical profession to make early diagnosis of this condition. In any event, restoration of a more normal circulation and a better balance of blood flow to all parts of the body should be of benefit.

The indications for and contraindications to operation in these cases at present are not clear cut. At present I believe operation should be considered for all patients who have evidence of severe coarctation regardless of age provided their general condition will permit an opera-

tion of this magnitude. I do not believe that patients who have already had heart failure or cerebrovascular accidents will benefit from operation sufficiently to justify the risk of surgical intervention. In general, the younger the patient the better the candidate for operation.

In conclusion, I should like to emphasize that coarctation is not as uncommon as is generally supposed. As has been pointed out, the diagnosis of coarctation is not difficult and does not require any equipment that is not available generally. The experience with surgical treatment of coarctation, while not extensive, is most encouraging.

REFERENCES

1. BLALOCK, ALFRED, and PARK, E. A.: The surgical treatment of experimental coarctation (atresia) of the aorta. *Ann. Surg.* 119:445 (March) 1944.
2. CRAFOORD, CLARENCE, and NYLIN, G.: Congenital coarctation of the aorta and its surgical treatment. *J. Thoracic Surg.* 14:347 (October) 1945.
3. GROSS, R. E., and HUFNAGEL, C. A.: Coarctation of aorta; experimental studies regarding its surgical correction. *New England J. Med.* 233:287 (September) 1945.
4. BLACKFORD, L. M.: Quoted by PERLMAN, LAWRENCE: Coarctation of the aorta: clinical and roentgenologic analysis of thirteen cases. *Am. Heart J.* 28:24 (July) 1944.
5. EVANS, WILLIAM: Congenital stenosis (coarctation), atresia, and interruption of aortic arch; study of 28 cases. *Quart. J. Med.* 2:1 (January) 1933.
6. LEVINE, S. A.: Quoted by PERLMAN, LAWRENCE: Coarctation of the aorta: clinical and roentgenologic analysis of thirteen cases. *Am. Heart J.* 28:24 (July) 1944.
7. LINDGREN, A.: Quoted by GLADNIKOFF, H.¹⁴
8. ABBOTT, MAUDE E.: Coarctation of the aorta of the adult type; II. A statistical study and historical retrospect of 200 recorded cases with autopsy, of stenosis or obliteration of the descending arch in subjects above the age of two years. *Am. Heart J.* 3:574 (June) 1928.
9. KING, J. T., JR.: Quoted by PERLMAN, LAWRENCE: Coarctation of the aorta: clinical and roentgenologic analysis of thirteen cases. *Am. Heart J.* 28:24 (July) 1944.
10. HAMILTON, W. F., and ABBOTT, MAUDE E.: Coarctation of the aorta of the adult type; I. Complete obliteration of the descending arch at insertion of the ductus in a boy of fourteen; bicuspid aortic valve; impending rupture of the aorta; cerebral death. *Am. Heart J.* 3:381 (April) 1928.
11. BONNET, L. M.: Sur la lésion dite sténose congénitale de l'aorte dans la région de l'isthme. *Rev. de méd., Paris* 23:108; 255; 335; 418; 481, 1903.
12. LEWIS, R. B.: Coarctation of the aorta with congenital bicuspid aortic valve and dissecting aneurysm of the arch of the aorta. *Am. J. Clin. Path.* 15:297 (July) 1945.
13. DAVIES, J. N. P., and FISHER, J. A.: Coarctation of the aorta, double mitral A-V orifice, and leaking cerebral aneurysm. *Brit. Heart J.* 5:197 (October) 1943.
14. GLADNIKOFF, H.: The roentgenological picture of the coarctation of aorta and its anatomical basis. *Acta radiol.* 27:8, 1946.
15. BRAMWELL, C., and JONES, A. M.: Coarctation of aorta; collateral circulation. *Brit. Heart J.* 3:205 (October) 1941.

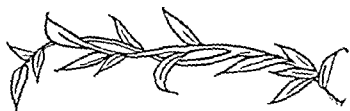
WOOLSEY APPOINTED SLICHTER RESEARCH PROFESSOR AT WISCONSIN

Dr. Clinton N. Woolsey of the Johns Hopkins University School of Medicine has been appointed to the recently created Chair, the Slichter Research Professorship of Physiology at the University of Wisconsin Medical School, according to an announcement made by Dr. William S. Middleton, Dean of the Wisconsin school.

Dr. Woolsey graduated from the Johns Hopkins School of Medicine in 1933 and has devoted himself to the field of physiology and neurophysiology at that institution since that time. He was Associate Professor of Physiology at the time of the present appointment to Wisconsin.

Dr. Woolsey's particular area of investigation has been the field of neurologic research in physiology, and he will continue his studies in the field of neurophysiology at the University of Wisconsin Medical School.

The Wisconsin Alumni Research Foundation established the Charles Sumner Slichter Research Professorship in the Natural Sciences in memory of the late Professor Charles Sumner Slichter. Dr. Woolsey is the first appointee to that Chair.



The Stuffy Nose

J. LEWIS DILL*

HENRY FORD HOSPITAL, DETROIT

THE SYMPTOM of a stuffy nose, which has always been a problem, still continues to plague us. I say a problem, for witness the number of patients who consult one physician after another attempting to find relief, only to turn to self-medication or neglect. Witness too the amount of nasal drops, sprays, and drugs such as benadryl and pyribenzamine, which have been prescribed by physicians and sold over the drugstore counters in the hope of obtaining a cure.

A stuffy nose, uncomplicated, requires much investigation before the diagnosis may be made. Unfortunately, it is too often a complex condition involving several diagnoses, calling for skill, judgment, and the combined efforts of the family physician, the rhinologist, and the allergist. The treatment may be rather lengthy and often may have to be revised or entirely changed. Each patient must be fully cognizant of the regimen to be followed so that the fullest cooperation may be obtained, and the treatment completed without interruption.

A person who presents himself to us with a stuffy nose often complains of a continuous or recurrent head cold, sinus trouble, a blocked nose, or inability to breathe. These symptoms

may be seasonal or perennial, and may vary from week to week, day to day, and often from hour to hour. Many such patients have a dull frontal headache, pains across the bridge of the nose, sneezing, and coughing. Many also state that they cannot blow anything out of the nose, but have an excessive discharge in the throat.

The question arises as to what we can do for these people and how we may undertake treatment to produce relief of their symptoms. In the beginning, a careful general physical examination must be given to each person. In an increasing number of instances allergy studies are required. Occasionally consultation with an allergist or psychiatrist may be necessary.

There are many underlying factors which must be considered before a diagnosis can be made. Briefly, I would like to enumerate and to comment on the more important causes and types of stuffy nose (these, however, are not arranged in the order of their importance): (1) adenoids, (2) sinusitis, (3) deflected nasal septum, (4) allergic rhinitis, (5) vasomotor rhinitis, and (6) irritative rhinitis.

ADENOIDS

Adenoids are present in the nasopharynx of practically every child and not infrequently in

*Surgeon-in-charge, Division of Otolaryngology, Henry Ford Hospital.



J. LEWIS DILL

the nasopharynx of the adult. This chronically infected mass of tissue not only produces an obstruction but also becomes a constant source of infection. In many children this adenoid tissue has a tendency to recur, even after an operation with what was felt to be a thorough removal of this tissue. Not infrequently an adenoidectomy has been only a partial removal, with a mass of adenoid tissue left high in the nasopharynx.

In this type a mother frequently brings in her child with a "runny" nose and an open mouth, complaining that he has a stopped-up or a stuffy nose not relieved by blowing. Often only a slight amount of discharge is obtained on blowing the nose. These children may have a dry and irritating cough.

Nasal examination discloses a discharge, either mucoid or mucopurulent, lying along the floor, a congested mucous membrane, and a nasopharynx almost completely filled with adenoid tissue. A nasopharyngoscope will show this adenoid tissue to be bathed in a discharge of the same type as that seen in the nose. Occasionally one sees a nasal mucous membrane

which is pale and edematous and resembles that seen in the late stage of an allergy.

Complete removal of this adenoid tissue under general anesthesia relieves the obstruction and banishes a focus of chronic infection with rapid restoration of nasal function.

SINUSITIS

Sinusitis should present no difficulty in either the acute or the chronic cases. Patients with a sinus infection have a stuffy or a blocked nose, a purulent nasal and postnasal discharge, and frequently a cough. The acute infection occurs during a head cold or following a tooth extraction, with accompanying pain or ache over the involved sinus, and an elevation of temperature. The nasal mucous membrane is acutely red, swollen, and congested, and the nose is filled with a purulent discharge. The involved sinuses are tender on pressure, dark on transillumination, and cloudy on x-ray. With suction, pus can often be traced to the orifice of the sinus, and with a nasopharyngoscope pus can be seen coming from the involved sinus.

Chronic sinusitis presents more or less the same signs and symptoms as seen in the acute cases; lacking are the acute signs of pain, tenderness, and elevation of temperature. Contrary to popular opinion, headache is rarely a symptom of an uncomplicated chronic infection of a sinus. The origin of the pus in the nose should always be determined by a nasopharyngoscopic examination.

TREATMENT in both chronic and acute sinusitis should be adequate to eradicate all infection completely. In acute cases we advise rest, plenty of fluids, heat to the affected areas (hot compresses, Simms' light, or infrared lamp), codeine for relief of pain, sulfa, penicillin, or both in adequate dosage, and irrigation of the involved sinus only when the infection fails to respond during the second or third week. In chronic sinusitis treatment should be decided only after a thorough investigation, preferably

by a specialist. Sulfa therapy and penicillin have been disappointing. Surgery still remains the method of choice to eradicate a long-standing chronic sinusitis.

DEFLECTED NASAL SEPTUM

Deflected nasal septum may produce a unilateral or bilateral stuffiness depending upon degree, type, and location of the deflection. Not infrequently the nasal stuffiness is more marked on the side opposite the deflection; in the early stages this is due to excessive ventilation and in the later stages to hypertrophy of the mucous membrane, particularly of the turbinates. These patients seldom have an excessive nasal discharge, but generally have an accompanying postnasal discharge and complain of stuffiness not relieved by blowing.

The diagnosis should present no difficulty. An operation removing the septal deflection as well as the hypertrophy of the mucous membrane should result in complete relief.

ALLERGIC RHINITIS

Allergy is perhaps the commonest cause of a stuffy nose, since we recognize that it may produce perennial as well as seasonal symptoms. The symptoms of allergic rhinitis vary markedly, but it is surprising how these symptoms, after a thorough and careful history, do fit into their niche. We recognize that there may be many allergens—pollens, foods, cosmetics, animal hair, house dust, bacteria, cold, and heat. Physical allergy such as that due to cold and heat must be recognized: sudden changes of temperature appear to be the precipitating factors, as is noted occasionally when a person steps out of a hot shower into a cold room.

These patients complain of sneezing, dull frontal headaches, often a stuffy feeling in their ears, a stuffy nose, and an excessive, clear, watery discharge which stains, rather than fills, several handkerchiefs daily. The nasal mucous membrane is reddened and congested. In my opinion, it cannot be distinguished from that seen in an acute infection, except in the late

stages, when the mucous membrane becomes pale and edematous, and fails to shrink with a vasoconstrictor. On cytologic examination the discharge, usually clear and mucoid, is found to contain a high percentage of eosinophils.

In many instances the diagnosis can readily be made, but with all patients the diagnosis should rest on a careful evaluation of all the data obtained after a critical history, including an allergy history, a complete examination of the ears, nose, throat, and sinuses, a complete allergy study including skin tests, and microscopic examinations of the nasal discharge.

Treatment should comprise elimination, substitution, and immunization; special diet, food special cases, and injections of specific sera. In house dust, it may be necessary to go into the home to determine the cause, and to gather dust in order to carry out specific treatment. Vaccines, made from the specific strains of bacteria to which the person is sensitive, should be tried. These vaccines have produced successful results in many patients, especially children.

A DEFINITE regimen of specific allergic treatment should be instituted, altered as the reactions and results demand. The first injection should be a greatly diluted dose, increased gradually at four-to-seven-day intervals until the maximum dosage is reached. The maximum dosage should be sufficiently great to relieve the symptoms completely. Injections of this maximum dosage are made at lengthened intervals, until the injections are given monthly and then continued for a period of four to five years. Benadryl and other allied drugs may be tried orally. In the majority of patients these drugs give relief, and for this reason they may be used as a diagnostic aid. These drugs should not be continued indefinitely and should never replace specific treatment.

VASOMOTOR RHINITIS

Vasomotor rhinitis is indistinguishable from allergic rhinitis in the signs and symptoms it



CHARLES A. GORDON

Though not consistently practiced during the course of cesarean section, here it is no less important and perhaps more so. If bleeding continues, its source may be found in the birth canal, and perhaps it will be necessary to draw down the cervix with sponge forceps. In any case, when uterine contraction is not well maintained, even though the placenta may have appeared to be intact, exploration of the uterine cavity should be prompt.

For an atonic empty uterus, the uterine pack may not be depended upon. If used at all, it should not be repeated, and decision to perform hysterectomy should be reached at this point. It should be obvious that transfusions of blood, no matter how large, will not save life if hemorrhage is allowed to continue. It is far more important to stop blood loss than to replace it.

It is well to keep in mind that rupture of the uterus accounts for about 6 per cent of our maternal deaths. Generally thought to be a rare accident, it surpasses ectopic gestation as a cause of death. Curiously, traumatic rupture in the

course of version or instrumental delivery fails of diagnosis in more than half of the cases, since the hemorrhage and shock associated with it are commonly attributed to embolism, to cardiac failure, or simply to the trauma of the operative procedure itself.

The uterus should be explored after every version and whenever shock after forceps delivery appears to be out of proportion to blood loss. Exploration should be painstaking, not perfunctory, for incomplete tears and rupture of the anterior wall may be missed. Although it may appear to be safer to await recovery from shock before laparotomy for rupture of the uterus, operation, supported by transfusion, of course, should be prompt.

Every physician knows that lost blood should be replaced, yet a complacent attitude toward hemorrhage and a hope that bleeding will stop lead to the administration of pitifully small amounts, or none at all, or use of substitutes that are nearly or wholly ineffective. Women in severe shock due to hemorrhage can be resuscitated only by whole blood, since reduction of their blood volume is due to loss of whole blood, not plasma alone. If shock continues long enough, no amount of transfused blood will save them.

PLASMA is but a sop to conscience and a sacrifice to convention when hemorrhage has been great. Not only does it have definite limitations, but, as a matter of fact, pooled plasma, so easily obtained at present, should not be used at all by obstetricians, since the risk of homologous serum jaundice is considerable.

The importance of whole blood transfusion cannot be overstated. Large amounts are often necessary, and the sooner blood is administered, the better. Speed during its actual administration is often vital. Several portals may be used at once, and when veins fail or cutdown is time-consuming or unsuccessful, the sternal route should be employed.

Shock may follow hemorrhage. Dehydration, long labor, and anesthesia will make significant contributions, and will often precipitate shock

when blood loss alone would not have done so. The best way to treat shock is to prevent it. Low blood pressure is not an early symptom, but slight decline in the systolic level is of great importance. Acceleration of the pulse is significant, but diminution in pulse volume is the earliest available clinical evidence of shock.

Saline and dextrose solutions are valuable in prevention of shock, yet they are not only ineffective but dangerous when shock has been established. Aqueous solutions will not be retained in the blood stream if plasma colloids

are insufficient to maintain volume. Postponement of blood transfusion is serious. Morphine and oxygen are helpful. Adrenalin is futile, perhaps harmful. All cardiac stimulants are contraindicated, since shock is not of cardiac origin.

Suitable blood must be available on the delivery floor, otherwise the lying-in hospital is not a safe place for delivery. And at that time the obstetrician must be ever mindful of the possibility of hemorrhage, aware that at any moment he may have to thrust routine aside and prove himself.



MULTIPLE MOTHERHOOD

The naive logic of the Dark Ages viewed multiple motherhood with moral abhorrence. Superstition ascribed to each child a different father. Thus, twins, triplets, etc., automatically branded a mother as a creature guilty of carnal waywardness.

Birth of Quintuplets. Water color by unknown Dutch artist. Quins and ballyhoo—200 years ago! Five children were born to the wife of a Dutch peasant in 1719 . . . and an unknown native artist immediately recorded the event for posterity. We see here the surprised father's first glance at the new arrivals. Four of the children died soon after but were not interred for several weeks due to the universal interest that forced the parents to exhibit the quins at a profit.

From: The Bettmann Archive

Major Defects of the Face and Their Surgical Repair

JAMES BARRETT BROWN AND MINOT P. FRYER*

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

IN CARING for a large volume of patients who need repair of major facial injuries, one of the things we think of is something we are all candidates for, and every member of our families is too—and that is a bad automobile wreck. This might lead to some feeling of the Golden Rule in our basic approach to the problems of each patient.

One fundamental is that almost unbelievably good results can be obtained if there can be prompt evacuation. These patients should be put back together at the earliest possible moment if they can possibly be gotten into the hospital. A few things that delay early operation are lack of evacuation or transportation to a place where they can be cared for; too much general shock, too much brain damage, a broken neck, in which instance too much manipulation may be harmful. Of course, if intoxicated, the patients are not done immediately, and if it is a child and the stomach is full of food or it

has just eaten, it is preferable not to get vomitus, which is bound to occur, over the operating field. Otherwise, with prompt evacuation, getting up in the middle of the night if necessary to do the work, the best results are obtained.

The boy in Figure 1 has extensive avulsion of the nose and about the lids and cheeks. Almost immediate operation has resulted in saving the distorted features and giving him his restoration in a single operative procedure. The natural protection of the eyeball, which is an intact lid, should be replaced in these patients immediately. It is miraculous how extensively faces can be destroyed without loss of vision. If the proper protection of the lids is restored promptly the vision is preserved, but if the lids are left away from the globes serious corneal damage often results.

Two things may be mentioned, predicated on the fact that the face does not develop primary gas gangrene. In the first World War there was the recommendation of doing curtaining débridements on all wounds; and in World War II—at least the first part of it—there was an idea of packing all wounds open. These two proposals were based on prevention of gas gangrene, but since the face does not develop it, neither of these procedures has much

*From the Department of Surgery, Washington University School of Medicine, St. Louis, Missouri.

This paper was prepared from the transcribed notes of a diagnostic clinic given by one of us (J.B.B.) at the St. Louis Assembly of the Interstate Postgraduate Medical Association of North America, October 14 to 17, 1947. It is a summary, given in thirty minutes, of salient points in the care of these severely injured patients. Specific lesions such as the support of bones in general cannot be covered in detail.



Figure 1. Traffic accident. Extreme tearing and displacement of soft parts, repaired in single operation. Immediate evacuation and prompt closure of wound may give normal contour and function, whereas secondary reconstruction may require multiple operations and not give as good final result.

application in the face (or in the hand). Certainly if a cutting débridement had been done on the boy's face in Figure 1 or if it had been packed open he would have required twenty to thirty operations to get anything as favorable as the result with his one immediate operation, and even then the flap repairs that would have been required would not be as smooth as the saving and replacement of the original local features.

Débridements of facial wounds are done, of course, but they consist of taking out gross dirt, getting the area as clean as possible, and removing hopelessly devitalized tissue. In trying to restore such damaged faces it can be said that "it is usually better to leave in some tissue that may die than to cut away some part that might live." The reason for doing this is that features themselves are being dealt with and general rules of débridement such as are applicable to the lower extremities simply do not fit in with the problem of salvaging the face.

PUTTING the displaced features, flaps, angles, and bones back together involves careful sorting of parts, usually starting at some

known margin or landmark for the fixation—picking out the lip or nostril, or eyelid border. If these landmarks are not made out, then correct fitting of a gross tear can be the start; following this bisecting the open areas with suture may tend to prevent final distortion, rather than closing right down a tear from one end to the other.

A *pressure fixation dressing*, using cotton surgical (or mechanic) waste, is one of the fundamentals of care, as important as the procedures of the operation. It is interesting that the first recorded use of pressure dressings was as far back as the hieroglyphics and was recommended for wounds of the face.

Another important element of early transportation is the control of hemorrhage, and getting it stopped before transportation. The patient in Figure 2 is literally bleeding to death in his own tissues. His wound has been closed but the local points of hemorrhage have not been stopped, and his wound is ballooned full of blood, there is pressure on his airway and it is apt to be occluded. It seems definite that hemorrhage should be controlled locally, that is, down in the wound where it is occurring. Ligation of neck vessels probably does enough

good to do it except in relatively few instances. This may differ from ideas expressed elsewhere, but if there were 100 patients who might possibly be considered for a neck vessel ligation, perhaps more damage would be done by doing all 100 of them than if none at all were done.

This patient's wound needs to be opened promptly and the bleeding points clamped, and ligated if possible. If the vessels cannot be ligated the clamps can be left in the wound and a dressing put on over and around them. Patients have been returned to the ward after operation with as many as 18 clamps left in place, surrounded by the pressure fixation dressing.

This man (Figure 2) has to have his hemorrhage controlled by opening the wound, and at the same time his face is opened the bones can be put back together. The lower jaw is shattered in about 12 pieces, and part of it is down in the neck. In this type of bone displacement it is still better to leave something in that might die than to cut out something that might live. There is just not any extra tissue in the face in these instances to allow for wide cutting débridements. Hopelessly detached flaps and chips of bone are of course removed, and this is most important around the alveoli and tooth sockets.

This patient's jaw was put back together after the bleeding was controlled, and the soft tissues were accurately closed with drainage. It looks like a crude procedure, but it has thrust his jaw forward and put his teeth back together and stabilized his jaw. This is an excellent instance of early evacuation, prompt control of hemorrhage, promptly putting the face back together, and putting on a pressure fixation dressing. This man has been able to assume his position as a minister following this

one single operative procedure. If this had not been done he would undoubtedly have needed a bone graft, plus skin graft lining put back into his mouth, necessitating multiple operations and long hospitalization.

The patient in Figure 3 illustrates the most direct method of putting in the bone graft. The graft itself is used for the splint so that no external appliance is used. Dental wiring and dental appliances are used on the inside when necessary or possible, but when firm wiring on both ends can be done the graft itself constitutes a splint because it is wired in so firmly that no further movement of the jaw occurs. Whatever teeth remain are locked in their normal position with interdental wires.

ON THIS patient is shown what is done on every patient. It is a pressure fixation dressing, and it is one of the most important steps of the entire operation. The pressure is finally obtained with the rolls of bandage and adhesive fixation, but the medium of pressure which gives a firm fixation is surgical waste incorporated in the dressing. (This waste is better than regular mechanic waste and is supplied by C. G. Walworth, Philadelphia.)

The patient is shown with the lining of his mouth having been made with a skin graft from the skin of his leg, a graft in his jaw, and a new set of teeth.

The patient in Figure 4 is a doctor who had his jaw shot away and his chin opened completely so that all his saliva drained out on his chest. He is shown to illustrate the use of all local tissue possible. The *sine qua non* of plastic surgery is to be able to put in new tissue, but whenever possible, what is locally available is used. A large flap for repair is not resorted to because it is felt that there is enough tissue

Figures 2a and b. Traffic accident. Patient with extensive shattering of bone and in extremis from blocked airway due to hemorrhage into wound, the edges of which have been closed. Prompt opening and local control of the bleeding is necessary. f and g. X-rays show extensive displacement of bone with immediate replacement and fixation at time of operation. Final view shows jaw with normal length and solidity. c, d and e. Final result obtained in the single operation with patient able to carry on duties as a minister. Delayed or secondary reconstruction would have required several operations including bone grafts. →

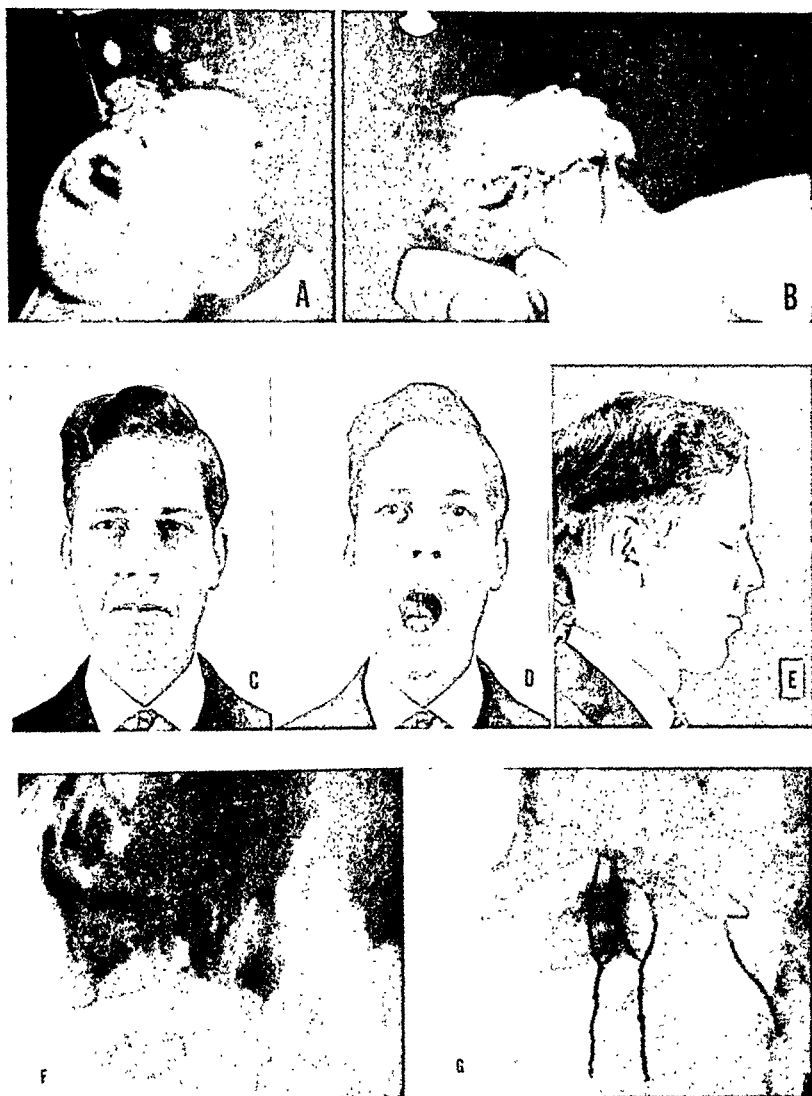
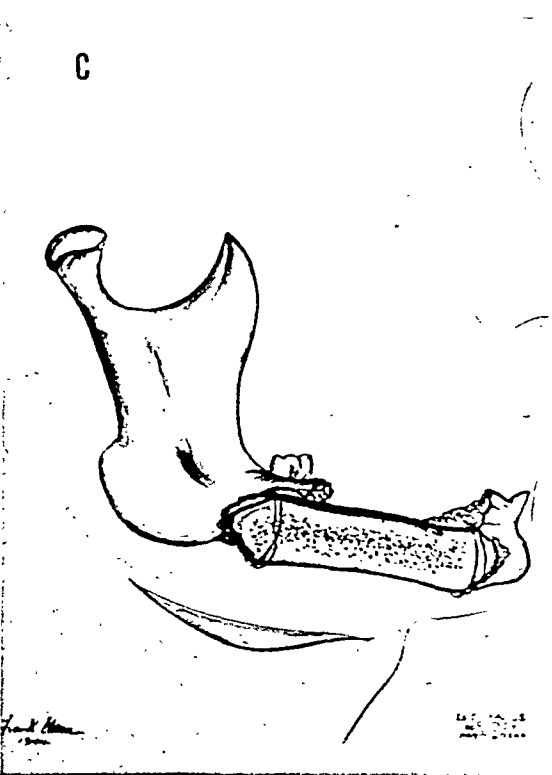
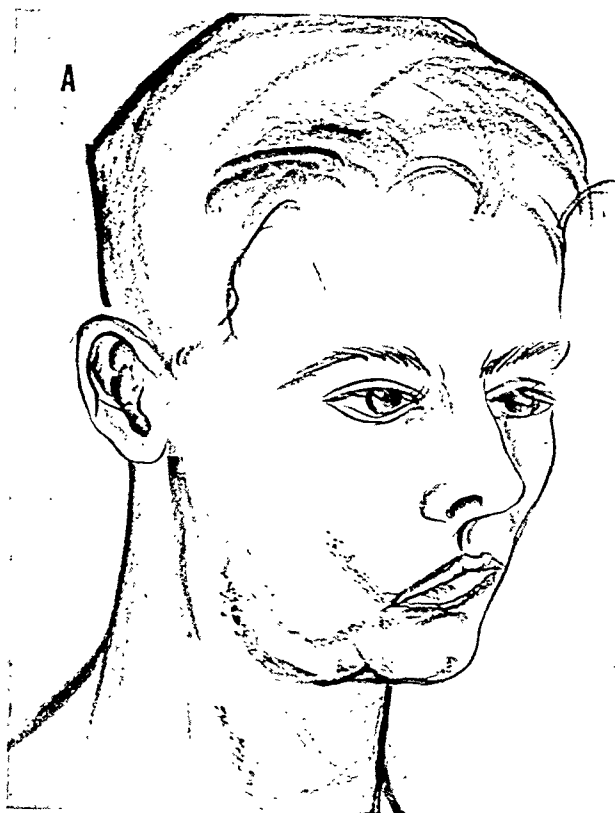


Figure 2.



Figures 3a and b. Gunshot injury. Extensive loss of substance including bone and lining of mouth. Patient seen after several weeks. Sequestrectomies skin graft for lining of mouth and bone graft necessary for reconstruction. c and d. Detail of bone graft, wired in place to form its own splinting, plus fixation of remaining teeth. Detail of fixation-pressure dressing using cotton surgical waste as the medium of pressure.



Figures 4a and b. Loss of substance of jaw and soft tissues permitting saliva to drain out on chest. Mobilization of local flaps and repair in one operation so salivary flow goes back into mouth. Bone support done at secondary operation, as the soft tissues on the outside have to be restored before the support has a place to go.

available for the closure, and in just one operation under local anesthesia the mouth is watertight, the saliva is going back down the patient's mouth, and he is ready to have his bone graft put in.

The man in Figure 5 is one who needs new tissue brought in for replacement of a gross loss. The first problem is to mobilize his tongue; it is shown fixed out on his neck, and he can't move it. He also has had to have a tracheotomy and a gastrostomy.

One of the problems to be realized is that these people are still individuals; this patient has a wife and a fine little boy at home and, without too much preachment, we feel that the doctor-patient relationship in these instances is as important as in any other branch of medicine or surgery. We do not know how a service can exist without starting down on that level and using some essence of the Golden Rule.

The tongue has been mobilized with a free skin graft off the neck placed under it so that it can be moved. A delayed flat flap across his chest has been prepared with skin from above the clavicle tucked down underneath the flap to form the new lining of the mouth when it is put up.

All local tissues have been used including

a large piece of displaced lip. When the flap is raised for use and is found to be satisfactory, the new defect is recreated; it is necessary to go back and do practically the same thing the missile did—open up all the tissues and recreate the defect. The parts have to be dissected back to their relatively normal positions to let the flap in, rather than pulling them together at this stage.

The chest is grafted by a different operating team, so the patient winds up with a closed wound instead of a large open area on his chest. The lining of the mouth is made by a turned in flap lining the main one.

The whole jaw from ramus to ramus has been put in by another single operation using a bent single piece of rib or formed piece of ileum. The plastic surgeon often has to build backwards—the outside has to be made before the support is put in. An architect would think this was impossible but a jaw bone can't be put in place when there is no place to put it, or no covering for it.

Figure 5c shows the patient ready to go back home. The work can be improved, but the patient is still an individual and he still needs all these elements of a face just as much as if he had never lost them. Although this patient does

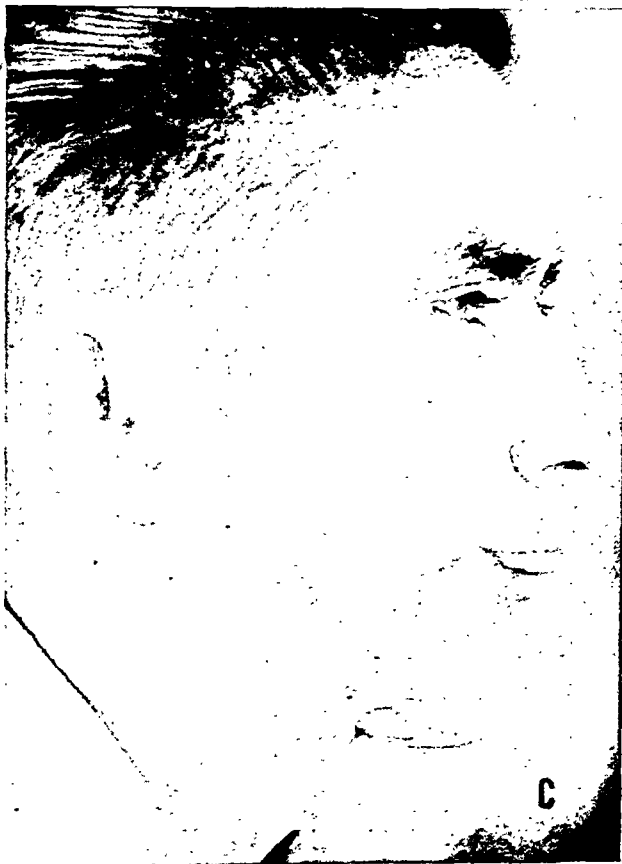
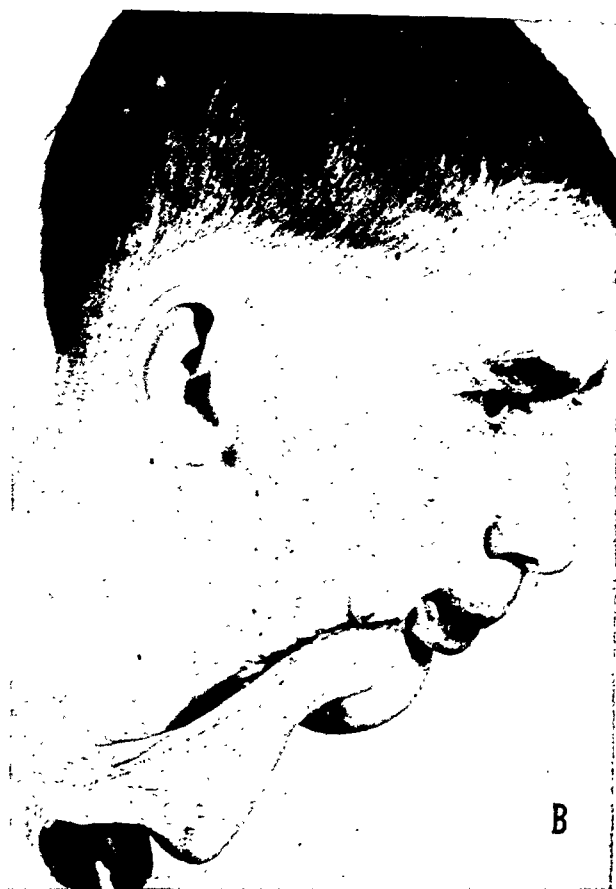


Figure 5. Details of extensive replacement of soft tissues and bone in multiple stage procedures, as outlined in text. (From Brown, J. B., and Cannon, Bradford: Repair of major facial injuries. *Ann. Surg.* 126:624-632 [October] 1947.)

not have any kinesis in his reconstructed area except what he produces by the upper part of his face, his jaw is forward and he can go on and again assume his way in life.

THE PATIENT in Figure 6 is shown with the replacement in one single operation of the entire ala of the nose with what we have called a "composite graft" from the ear, that is, two surfaces of skin with the intervening cartilage. The repair is more adequate than any other type, and the saving to the patient of from three to ten operations by getting it done in one operation is another big item.

Figure 7 shows a little of the technic. The dissection of the wound has to go back to an

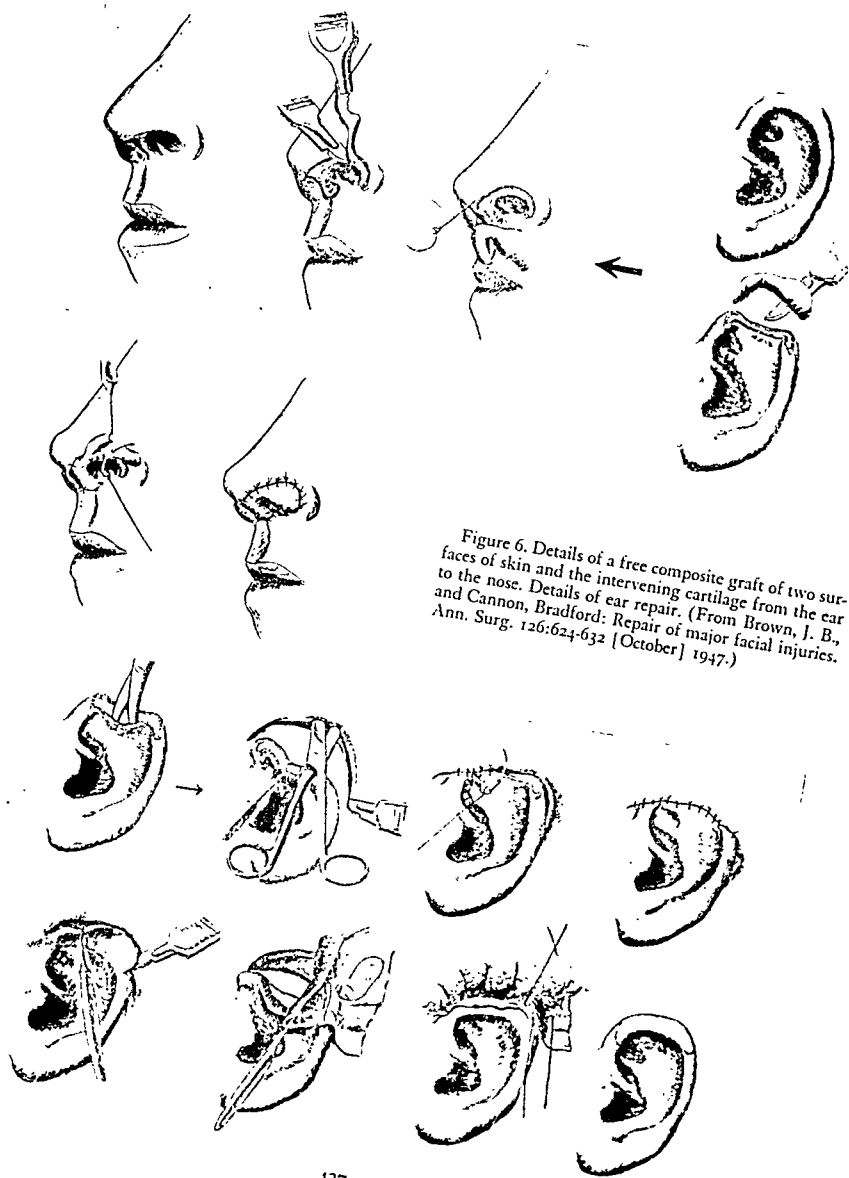


Figure 6. Details of a free composite graft of two surfaces of skin and the intervening cartilage from the ear to the nose. Details of ear repair. (From Brown, J. B., and Cannon, Bradford: Repair of major facial injuries. *Ann. Surg.* 126:624-632 [October] 1947.)

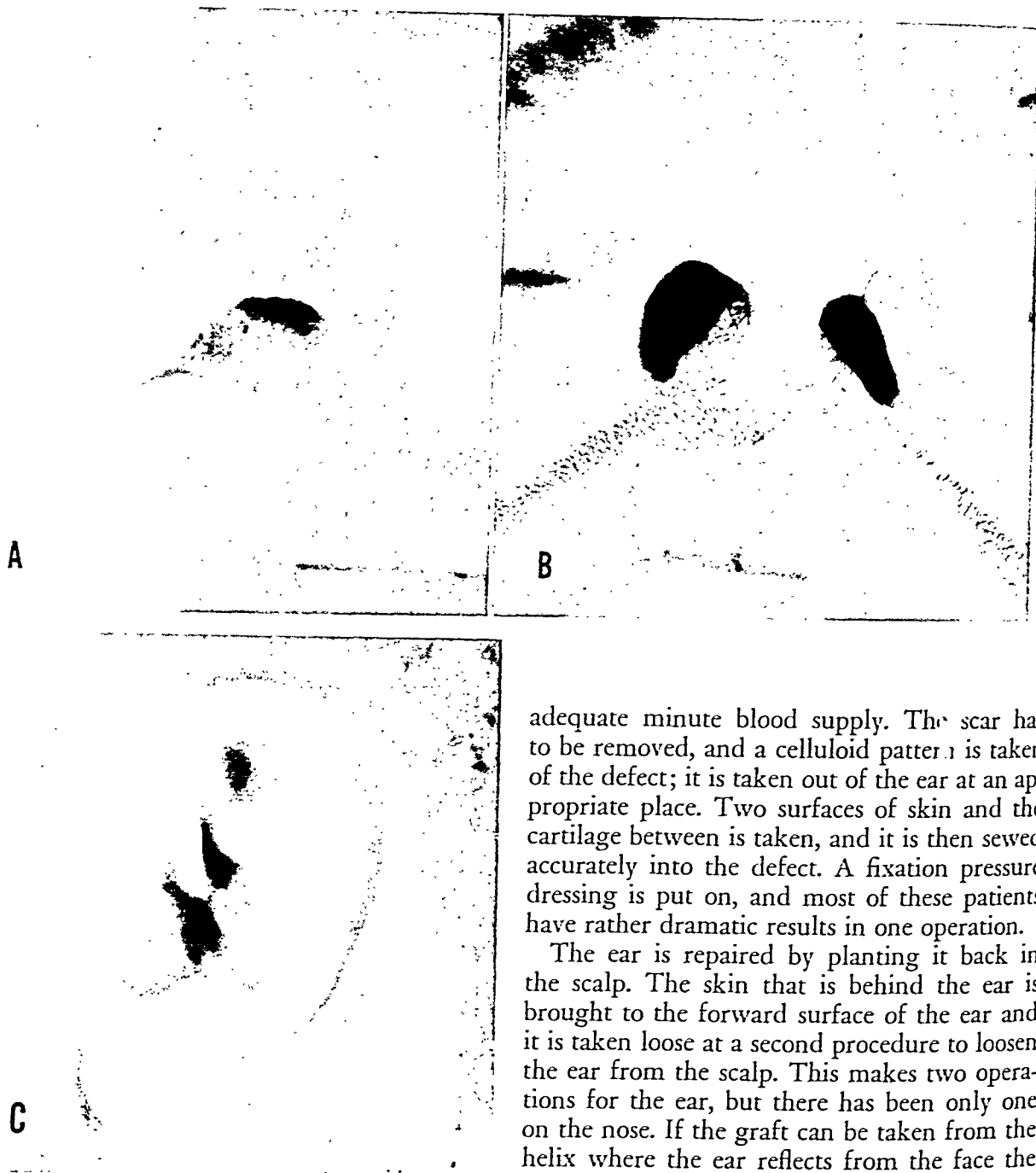


Figure 7. Single operation for restoration of ala, angle, and columnella of nose with free composite graft from ear. The repaired ear is shown. The lip has been let down from up in the nostril by a single operation using a free graft from the clavicular region. (From Brown, J. B., and Cannon, Bradford: Repair of major facial injuries. *Ann. Surg.* 126:624-632 [October] 1947.)

adequate minute blood supply. The scar has to be removed, and a celluloid pattern is taken of the defect; it is taken out of the ear at an appropriate place. Two surfaces of skin and the cartilage between is taken, and it is then sewed accurately into the defect. A fixation pressure dressing is put on, and most of these patients have rather dramatic results in one operation.

The ear is repaired by planting it back in the scalp. The skin that is behind the ear is brought to the forward surface of the ear and it is taken loose at a second procedure to loosen the ear from the scalp. This makes two operations for the ear, but there has been only one on the nose. If the graft can be taken from the helix where the ear reflects from the face the ear repair is done immediately so that there is but one operation on the ear.

This total replacement of a defect in a single-stage procedure is dwelt on because most plastic surgery is thought of as being long, drawn-out work with multiple procedures. Actually there is not relatively much operating, even in the preceding patient in Figure 5 who had only three major operations. But the waiting periods

between the operations take time. One cannot rush nature in the healing. When trouble occurs it is often found that some procedure has been hurried along. When in doubt, the process should be delayed to be safest with the all-important blood supply.

It can be seen that there is a skin graft on this patient's lip. To start with the lip border was clear up in the nostril. The first operation was to let his lip down and repair the defect with a full-thickness graft from just above the clavicle. The skin from this area is the most ideal type of skin with which to repair faces. It has a face-like quality, it can be transferred quite thick, its function is excellent, and its color is the best for the face. Another good source for color and function of grafts is behind the ear, but the quantity available from both of these sources is naturally limited.

Much of plastic surgery is predicated on the repair of defects from the treatment of carcinoma. These instances are usually in older persons who have some loose extra tissue in their faces. But young people who need plastic surgery, especially in military surgery, do not have any extra tissue in their faces, and so in making repairs for them it is felt that no further damage should be done to the face if it can be possibly avoided. Naturally all local tissue possible is used, but not at the expense of adding other gross deformity or scar or interrupting important nerve supply or function.

There is usually not too much trouble in taking the arm or neck or some distant area to repair these badly damaged faces, for example in making noses. Instead of cutting into the forehead and damaging it to some extent, the nose can be rebuilt with an arm flap. If the color is not adequate, permanent pigment injection can be done and the nose tattooed to be a decent matching color.

Extreme burns of the face form a whole chapter by themselves, and they occur by the hundreds. The main point in military surgery especially, is that they come in, "blown" full of dirt, and suffering all degrees of general debility, chronic shock, and malnutrition. What can be done for persons like this? We

have simple, philosophical basic rules. What these patients need is to "get the wounds as clean as possible as soon as possible and to restore what skin has been lost." The patient in Figure 8 has had all of his restoration with split skin grafts. Total healing has been obtained and although he is not completely normal looking, he has good function, and is able to get by this way as co-captain of a football team and is able to play football. He has had both ears made, most of his scalp grafted, and much of his face grafted. Incidentally, he has been married and has become the father of a little boy since this happened.

THERE is a problem about a burned male face which the female does not have, and that is the caught whiskers. Many whiskers are caught under the surface and if they are not thoroughly burned out, they become imbedded in these very bad scars, and for restoration there has to be complete resection of the area to get rid of the hair follicles.

When these patients heal they are miserable because they do not have enough skin left to move around in. It is as if one had on too tight a pair of gloves or pants and could not move. These patients do not have enough skin for normal movement of the face. What do these patients need? The same thing just mentioned—"put back what has been lost," but first we have to recreate the original defect or loss to put his tissues, his eyelids and his nose and lips back where they belong. Too much pulling around of remaining tissues in the face only creates more deformity. Unfortunately the buried whiskers go clear through the skin down into the subcutaneous tissue, and a relatively deep dissection has to be done.

An important question in most severe facial burns is whether a pedicle flap such as in Figure 5 or free skin grafts should be used. Practically every burn can be done with free grafts on the flat surfaces and eyelids. Even the nose can be done if there is good enough support or armature left; if not, a pedicle flap repair is utilized.



Figure 8. Extensive loss of skin from burns with restoration with free grafts and local flaps for ears.

The results of treatment of carcinoma cause many extensive defects of the face and one illustration is shown in Figure 9. This patient has had an invasive basal cell carcinoma of the orbital region. Basal cell carcinoma is in no wise the mild growth that it is sometimes said to be in text books. It is questionable that invasive basal cell carcinomas are often cured if they have gotten in deeply enough. This is not intended disparagingly or hopelessly, but it is mentioned to suggest that these growths be considered dangerous and refractile to treatment and cared for early and thoroughly.

Perhaps the most dangerous place one could have such an invasive growth is at the orbit. The next most dangerous is around the ear, and the third most dangerous is the pyriform recess beside the nose.

An exenteration has been done with nothing left in the orbit in the patient in Figure 9. The

repair has been made with a direct flap from the forehead so that only two operations were necessary. Many times delayed flaps are used but in this instance the orbit is covered with this part of his forehead brought down as an immediate or direct flap. The flap is severed at a later date and the forehead is repaired with a graft from his leg.

Perhaps one might say, "Why not make a new orbit?" The answer is that at present, good enough orbits are practically not obtainable with the extensive work that they require. If kenesis of the new lids cannot be obtained, then one cannot get an orbit which will retain an eye. If this is the outcome the patient won't go without a bandage anyway, so that he is usually much better off with this blanked-out procedure and he can go immediately about his business. Any type of artificial prosthesis can be made but patients seldom wear them



Figures *a*, *b* and *c*. Invasive basal cell carcinoma resistant to local excision. Recurrence shown requiring total obliteration of orbital region. Direct flap



from forehead used for repair. Two operations, *d* and *e*. Blanked out orbit, free of trouble and of dressings. Nine years with no recurrence.



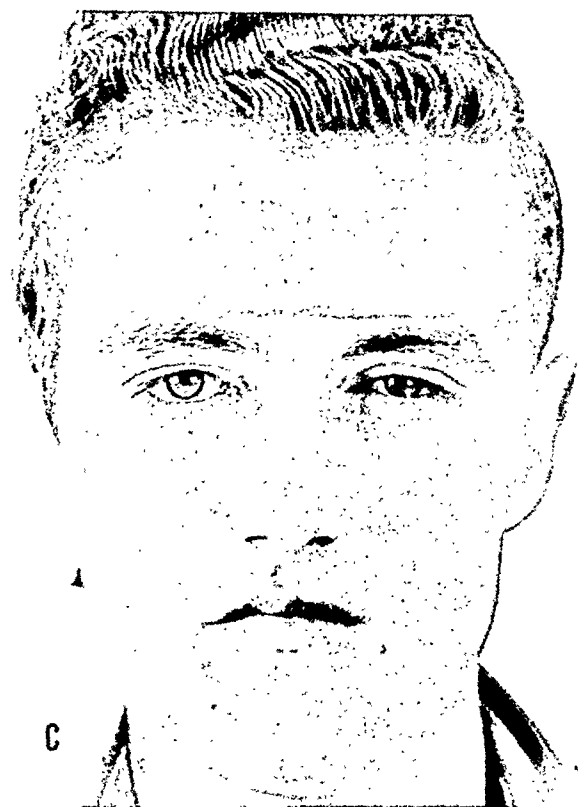
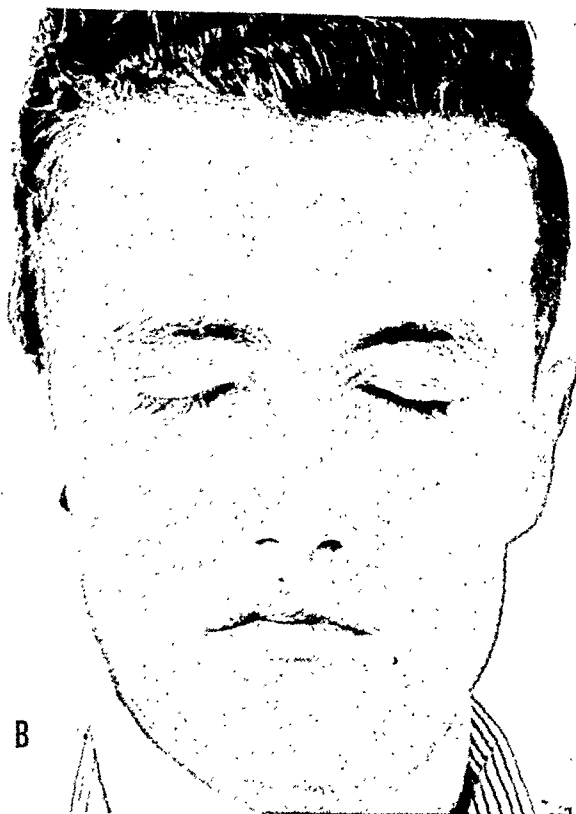
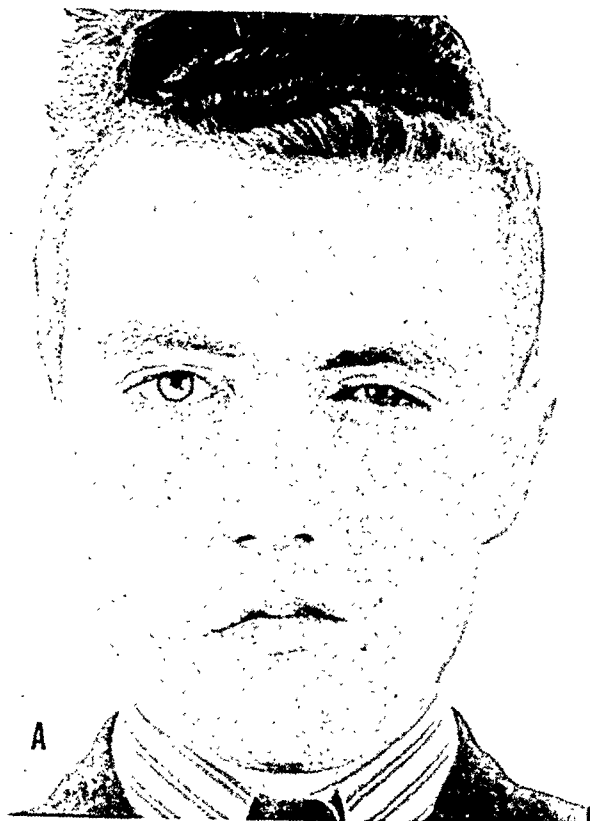


Figure 10. Facial paralysis supported with strips of fascia lata anchored in the temporal muscle. Patient completely closes eye (which is not always obtainable) and gets by with many who see him not realizing his seventh nerve is paralyzed.



Figure 11. Whole face and nose pushed back or caved in, from traffic accident. Patient was seen late when bones were firm in depressed position. Whole face built forward with four cartilage transplants, both orbital borders, across under nose from side to side, and L-shaped transplant for dorsum of nose and columella.

consistently. This patient has gone nine years without recurrence.

FACIAL paralysis, of course, would be ideally repaired by nerve repair, but when there is no chance of nerve restoration—or while awaiting a decision about it, the face can be supported by live strips of autogenous fascia lata. These are anchored in the temporal muscle and fascia and down in the face at the mouth and lip level. Strips may be put through the lower lid if necessary and in long-standing instances with much loose lax tissue this can be elevated and excised. The patient in Figure 10 illustrates this method of repair. From a total, obvious paralysis, he has the support of his face from a fifth nerve muscle and by not overacting on the sound side, he can get by with most passers-by not realizing that his face is paralyzed. By elevating his face he also can close his eye, but this degree of function is not always obtained.

Severe crushing injuries of the face may practically destroy all bony continuity and leave the bony structure in dozens of pieces without doing much permanent soft tissue damage. For the early replacement of the bone, practically everything should be saved and put back into position in procedures that are aimed primarily at "doing the opposite of what the accident did." Soft comminuted bones are packed or "mulched" into position and held with gauze packs inside the nose and antra. External fixations and appliances, and the proper fixation of the teeth are carried out as required.

When facial bones are left out of position for too long a time, they become fixed and cannot be successfully shifted and retained in position. In these instances subcutaneous prostheses are used, usually as transplanted cartilage or bone, or some persistent non-irritating metal or plastic material.

The patient in Figure 11 shows a retruded face from a serious blow with not much semblance of his original appearance left. His restoration consists of cartilage transplants, across under both orbital borders to restore their prominence, a block of cartilage across under

the ala of the nose from side to side, and an L-shaped cartilage restoration of the bridge of the nose to bring it forward.

"The surgeon like the tailor can make no better cloak than his cloth and it is well to realize limitations as well as possibilities in attempting major repairs. There is only one original and more surgical restorations are only substitutions. Diagnosis is of major importance and includes determination of what tissue has been lost or displaced as well as what distorted function to expect from it.

"It has been firmly established that if badly lacerated faces can be restored promptly, that the one single operation can often effect an excellent result"—without early evacuation and early operation, satisfactory results can be obtained only with extensive procedures, requiring multiple operations.

REFERENCES

1. BROWN, J. B.: Fractures of the bones of the face. *Surg., Gynec. & Obst.* 68:564, 1939.
2. ———: The management of compound injuries of the face and jaws. *South. M. J.* 32:136, 1936.
3. ———: Fractures of the Jaws and Related Bones of the Face. Chapter XII. The management of fractures, dislocations, and sprains, by J. A. Key and H. E. Conwell. Springfield, Illinois, The C. V. Mosby Company, 1938.
4. ———, and McDOWELL, F.: Internal wire fixation for fractures of the jaw; preliminary report. *Surg., Gynec. & Obst.* 74:227, 1942.
5. ———, and ———: Internal wire fixation of jaw fractures; second report. *Surg., Gynec. & Obst.* 75:361, 1942.
6. ———: Compound Facial Injuries. Chapter IX. Surgical treatment, by F. W. Bancroft and G. H. Humphreys. Philadelphia, J. B. Lippincott Company, 1945.
7. ———, and CANNON, BRADFORD: Repair of major facial injuries. *Ann. Surg.* 126:624, 1947.
8. ———, and ———: Full-thickness skin grafts from the neck for function and color in eyelid and face repairs. *Ann. Surg.* 121:639, 1945.
9. ———, and ———: Composite free grafts of skin and cartilage from the ear. *Surg., Gynec. & Obst.* 82:253, 1946.
10. ———: Further reports on the use of composite free grafts of skin and cartilage from the ear. *Plastic and Reconstructive Surgery* 1 (No. 2):139, 1946.
11. ———, and CANNON, BRADFORD: Composite free grafts of two surfaces of skin and cartilage from the ear. *Ann. Surg.* 124:1101, 1946.
12. ———, ET AL: Surgical substitutions for losses of the external ear; simplified local flap method of reconstruction. *Surg., Gynec. & Obst.* 84:192, 1947.
13. ———: The utilization of the temporal muscle and fascia in facial paralysis. *Ann. Surg.* 109:1016, 1939.
14. ———, and McDOWELL, FRANK: Support of the paralyzed face by fascia. *J.A.M.A.* 135:118, 1947.

Physical Exercise in the Treatment of Hypochondriasis

WALTER FREEMAN*

WASHINGTON, D. C.

Mrs. Betty S. consulted me December 3, 1945, and I had to write pretty fast to keep up with her complaints. She dated her trouble from January 1944, when she had a hysterectomy, followed by catheterization, and supposed perforation of the urethra. She was going to sue the hospital. There had been two previous pelvic operations. Her husband stated that she had been full of complaints for years and had been unable to do any work around the house since 1942. She was 37 years old and had one child, and the domestic situation was far from serene.

"After that my body started to burn and there was so much discharge, bleeding, and pain in the groin. I went to ——— Hospital where a diagnosis was made of traumatic neuritis of the ilio-inguinal nerve and this resulted in complete paralysis of the left thigh. The infection spread to both kidneys and blocked the outlet, and a month ago Doctor ——— advised nerve block. When I go to get injections for my uterus, it seems to stir up the nerves. When the kidney works, it bothers me and I shake and quiver. In March 1945, my urethra was transplanted and I was desperate, it made the whole family desperate. I used to be very heavy but I've lost a lot of weight. I feel a contraction, feel all choked up, my leg draws and throbs, and my

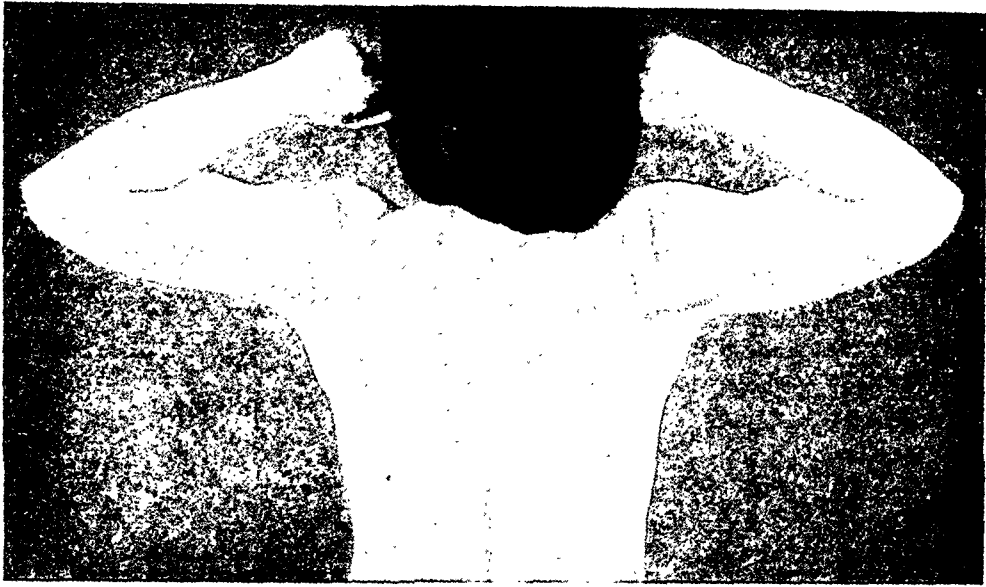
thighs seem to work. My head draws and my sides swell up."

Betty was animated in listing her complaints and she went into considerable detail, much of which I missed. The description was on the chaotic side and accompanied by a great deal of emotional display. Neurologic examination disclosed no defects in coordination, motor power, or sensibility. Blood pressure was 140/95 and the pulse 112. She showed marked hyperventilation, with cold hands, but no swaying in the Romberg test.

The husband agreed with the doctors that it was all in her head and this made Betty mad because she was sure there was something wrong, and she sat around and brooded all day and did no work in spite of her strong and healthy appearance.

My report to the referring doctor was that Mrs. S. might have some local condition that was potentially annoying, but it could not have been built up into all this high-powered extravaganza of symptomatology without a lot of emotion. Her hypochondriasis, I suspected, was rather firmly fixed but since I had seen even worse cases recover when their will power was challenged, I challenged the patient to come back to me in a week and prove that she had walked an average of five miles a day. I told the doctor that it would probably take her a long time to walk off the hypochondriasis, if she ever succeeded, but I was sure that shock

*Professor of Neurology, The George Washington University School of Medicine, Washington, D. C.



Patient described in Case Report.

therapy would never touch it and that prefrontal lobotomy was not advisable because of the strained domestic situation. I told her husband to stop telling his wife there was nothing wrong with her because a lot was wrong; but that he could help her by getting out and working and walking with her, especially on weekends.

Betty accepted the challenge. She started gradually so as not to get blisters on her feet; took her walking program seriously and in three weeks reported that she was up to ten or eleven miles a day, which I disbelieved. There was no cessation of the complaints; in fact, whenever she was allowed to, she started off again with a full series.

My next contact with her was through a summons served on me in her malpractice suit against the hospital. She sued the hospital for negligence and required my testimony. I was not summoned as an expert and was not allowed to testify as to my opinion because I had examined her and consequently knew something about her. I received the \$2.00 witness fee. She was awarded some \$5,000 from which the company appealed.

Meanwhile, she asked the referring physician to send her back to me, in spite of the fact that she thought I didn't like her. I confirmed him in this belief and told the doctor that I would receive his albatross, Betty, with considerable reluctance. She

came, nevertheless, and reported that her activities had been interfered with because of bad weather and illness in the family. However, in addition to walking, she exercised indoors by lifting weights, doing sitting-up exercises, running up and down stairs and when the weather was good she rode a bicycle or spaded up the garden. In the spring, she was accustomed to meeting the postman regularly on his route and he offered laughingly to give her a job. Her complaints were somewhat less severe than they had been six months previously, but had not changed in character.

In September 1946, things came to a show-down between the patient and her family because of her husband's objection to the strenuousness of the exercise. "No woman ought to be going through those calisthenics and weight-lifting exercises like she is. She'll hurt herself somehow and make it worse than before." When Betty began her recital it was very much like the same record played over again. "My nerves jump; water seems to come up to my knees and eyes; it burns in my head and my eyes; and I'm weak all over." She looked the picture of vigorous health. On one of her recent panicky spells she had been given some capsules, took them all at one time and was knocked out

for four days. The heart and blood pressure were normal and I insisted on her continuing her activities.

The panicky spells continued and on the occasion of her mother's death in December 1946, she became so upset that a physician knocked her out with morphine. She slept for four days and missed the funeral. She resumed her physical activity when she returned and achieved a sufficient relief of emotional tension so that she could again respond sexually to her husband better than she had for five years. Occasionally, when she got far enough away from civilization, she would pick up a big stick and pound the ground with it to get the tension out of her system. She accepted my suggestion to go bowling and to name the pins after her pet peeves, No. 1 being her husband. She soon excelled in the sport.

By this time she paid little attention to her husband's sneering attitude and went ahead with her muscular development. The trainer in a physical-fitness institute that she patronized estimated that she was doing the equivalent of 16,000 to 18,000 foot-pounds per day. Her muscular development in May 1947 is shown in the accompanying photo.

When seen in January 1948, she demonstrated her prowess by carrying me pick-a-back. She did not complain of her pelvic distress, in fact it was difficult to persuade her to talk about it. Instead she talked at length about her exercises and the control she was able to exert over individual muscles. She was sleeping well, enjoyed her activity and reported that her husband's attitude did not bother her now that she knew she was on the road to

health. Her suit had been settled for \$1,000, which paid for her operations with nothing left over.

COMMENT

Fundamentally, I believe that this was a case of hypochondriasis based on sexual disharmony and treated ineffectively by multiple pelvic operations. The financial settlement did nothing to eliminate the complaints. The physical activity régime undertaken by Betty some two years ago had three therapeutic effects: It compensated for the emotional hyperventilation by greatly increasing carbon dioxide production and thus restoring the balance. This was at the psychological or biochemical level.

In the second place, she was able to release her pent-up hostility by pounding the ground with a big stick, bowling, and lifting the bar bells. Finally it has shifted the focus of her attention from the unknown internal organs with their dire threat of disaster to easily visible and palpable structures, her muscles, in which she can take a certain pride. She has regained her good humor and her working capacity around the house and has planned to divorce her unsympathetic husband as soon as her son graduates from school.

SUMMARY

A case of severe hypochondriasis, malignant hyperventilation, compensation neurosis, and sexual maladjustment. The patient developed a single asset, her muscles, with good results.

MENTAL HYGIENE FELLOWSHIPS ANNOUNCED

POSTDOCTORATE research fellowships in mental hygiene will be awarded by the U.S. Public Health Service to qualified individuals holding a doctor's degree in medical or related fields. The fellowship carries a stipend of \$3,000 (\$3,600 for doctors with dependents), but not including tuition. A special research fellowship is also offered to those who qualify for a post-doctorate fellowship and in addition have demonstrated outstanding ability or possess specialized training. This fellowship does not carry a set stipend, the amount being determined in the individual case.

Additional information may be obtained from the Division of Research Grants and Fellowships, National Institute of Health, Bethesda 14, Maryland.

CLINICOPATHOLOGIC CONFERENCE

Pulmonary Infiltration with Adenopathy

FROM NICHOLS VETERANS ADMINISTRATION HOSPITAL*

HAROLD GORDON, M. D., EDITOR

CLINICAL ABSTRACT

THE patient, a 24-year-old colored male, was admitted July 16, 1947, because of pain in his stomach and the right side of his chest. He had been well until June 1945, when he had "gas on his stomach," usually accompanied by vomiting after almost every meal. He had only slight pain but his bowel movements became irregular. He entered a hospital, where no definite lesions were found, but his symptoms persisted. Later in 1945, he apparently had pleurisy with effusion and again entered a hospital. He did not know whether or not a diagnosis of tuberculosis was made. He stayed in the hospital six months, then was discharged from the Army and sent to a Veterans Administration hospital, where he remained another six months. Afterwards, he had soreness in the anterolateral portion of the right side of his chest, aggravated by deep breathing and coughing. One month before admission he was advised to enter a hospital.

His past history was non-contributory. He served in the E.T.O.

Physical examination—His admission pulse was

100, his blood pressure 120/70, his temperature normal. Several discrete, rather firm swellings, each approximately 1 to 1.5 cm. in diameter, were palpable bilaterally at the angles of the jaws and in the region of the parotid glands. There was slight limitation of expansion of the right side of the chest. The percussion note over the lower half of the right lung was impaired. A few râles were audible in the same region, with diminished tactile and vocal fremitus. There was marked tenderness in the right hypochondrium. The liver and spleen were not enlarged.

Course—He was afebrile except occasionally in the afternoon, when his temperature reached 99.2°. The pulse rate was in keeping with the temperature curve. Eleven days after admission he had some discharge from the urethra. A diagnosis of gonorrhea was confirmed by bacteriologic examination. Penicillin therapy caused prompt recovery. His course otherwise was not remarkable. A biopsy of one of the nodules at the angle of the right jaw was taken August 4. His status afterwards was that of an ambulatory patient.

X-ray reports—The pleura at the right base is thickened. The right lung shows spotty infiltration and the hilar shadow on the right side is increased. The left lung shows slight fibrosis. Two weeks later (July 29) the hilar nodes were enlarged bilaterally, otherwise no additional changes were seen. Gastrointestinal series and x-rays of the carpal and metacarpal bones showed no lesions.

*From the Departments of Medicine, Surgery and Laboratory Service, Nichols Veterans Administration Hospital, Louisville, Kentucky.

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Laboratory reports—Erythrocyte and leukocyte counts were within normal limits, as were hemoglobin values and the differential leukocyte counts. Sedimentation rate was 13 mm. per hour on July 17, 25 mm. per hour on July 29. The Kahn test on his blood was negative. A Mantoux test, July 21, was reported faintly positive. The serum proteins were 6.8 gm., with albumin 4.4 globulin 2.4. A later specimen contained 5.2 gm. protein, 2.4 gm. albumin, and 2.8 gm. globulin. Thirteen specimens of sputum (24-hour specimens, concentrated) and three gastric washings were negative for acid-fast bacilli. Urinalyses were not abnormal.

DISCUSSION

DR. J. MURRAY KINSMAN (Senior Medical Consultant): Certain things stand out in this man's history. He is a Negro in his early twenties. His illness started with pain in the stomach and pain in the chest. He had hardly any fever while in the hospital. He had no leukocytosis, and the sedimentation rate of his blood was elevated only slightly. In other words, he had very little systemic reaction. It is significant also that his serum proteins, at first essentially normal, later showed a reversal of the albumin-globulin ratio. He also had enlarged lymph nodes, with apparently the preauriculars being especially involved. I presume the diagnosis in this case revolves around the report on the biopsy.

The fact that the conference depends upon the report of the biopsy immediately calls attention to the lymphadenopathy. One of the first things to eliminate, therefore, would be some type of local infection, such as an infected tooth or sinus. That would have been likely if only the lymph nodes were being considered. But this man also had pulmonary symptoms and x-ray changes in his chest. I'd prefer to see the x-ray films demonstrated later because I believe that the abstract alone will permit us to make a diagnosis.

We can easily rule out local infection, such as an abscessed tooth, because he had symptoms of disease elsewhere. Next we might think of some of the blood dyscrasias. He had no anemia and no leukocytosis. The differential leukocyte counts were normal. The spleen was not enlarged and he

had no hemorrhagic manifestations. Accordingly, leukemia can be ruled out. Hodgkin's disease can be eliminated on similar grounds, plus the absence of generalized glandular enlargement and fever. These considerations also exclude the lymphomas.

According to the description in the abstract, the lung parenchyma as well as the hilar nodes were involved, so there is little suggestion of any of the lymphomas. These sometimes involve the throat and tonsils so we have to think of them. But I am assuming that this man had one disease, so I give equal weight to the pulmonary symptoms, the digestive complaints, and the enlarged nodes.

Next we might consider some of the acute infections, systemic rather than localized. Among these I include infectious mononucleosis. But this man had little fever, no generalized glandular involvement, no sore throat, no enlargement of the spleen, and no changes in the leukocyte counts or in the blood smears. The heterophil agglutination test was not done. There seems no indication for it.

NEXT we think of some of the chronic infections, especially tuberculosis. No acid-fast bacilli were found in the sputum or in the gastric washings. The changes in the lungs, as recorded in the abstract, are suggestive of tuberculosis but are by no means typical. It is my understanding, also, that the infiltrations seen by x-ray are more apt to start in the hilar region and spread laterally in Negroes than in white people. The lymph nodes often are involved in tuberculosis. But there are these potent arguments against tuberculosis—the patient had hardly any fever, he apparently did not feel very sick, the sedimentation rate was elevated only slightly, he did not have an increase in either lymphocytes or monocytes. I think tuberculosis is the second most likely diagnosis but it is not my diagnosis. Syphilis also has to be taken into account. It causes lymph node enlargement and occasionally produces changes in the lungs. However, in syphilis the lymph node involvement is usually generalized and the Kahn test on the blood is positive. It is hard to say more about syphilis. Like tuberculosis, it may affect almost any organ, so we have to consider it.

Perhaps there are other conditions we might



Figure 1. P-A film, showing bilateral hilar adenopathy with nodular reticulation in both lungs. There is also some infiltration in both mid-lung fields, extending from the hilum on each side, more marked on the right.

think of, but finally we come to the disease which I think this man had—Boeck's sarcoid, or sarcoidosis. As most of you know, this is a disease so closely allied to tuberculosis that many pathologists and clinicians believe it is a form of tuberculosis. It may involve almost any organ. Recently I saw an autopsy report in which lesions were found in the spleen, lungs, lymph nodes, skin, bones, liver, heart, and intestines. The skin is said to be affected in about 50 per cent of all cases. As far as the lymph nodes are concerned, the disease has a special predilection for the pre- and postauricular

nodes. That influences me in this case. The parotid and other salivary glands and the eyes are involved often, so that we speak of uveoparotid fever. The patient usually has fever when the parotid glands and uveal tracts are affected. When there is no uveoparotitis, the course may be afebrile, or nearly so. The absence of severe systemic reactions, such as fever, leukocytosis, and an elevated sedimentation rate, are in favor of Boeck's sarcoid. Incidentally, may I ask this—how sick was the patient?

RESIDENT: He has been discharged, but he never was really sick while in the hospital.

DR. KINSMAN: That fits in perfectly. Finally, pulmonary involvement is very common in Boeck's sarcoid. The pulmonary involvement may be of two kinds. In one, the hilar nodes become enlarged. In the other, the lungs present a speckled or spotted appearance. One thing here unusual in Boeck's sarcoid is the history of pleurisy.

To return to the patient we are discussing you will note he had a reversal of the A/G ratio. I am sure the staff men had sarcoidosis in mind, or they would not have ordered the test, especially a repeat examination. Apparently this man did not have any punched-out areas in the phalanges or metacarpal bones. At least, the x-ray report does not mention such lesions. I believe that it is very uncommon to see skin, lung, and bone changes all at the same time.

In summary, I base my diagnosis of sarcoidosis on these considerations: The patient is a Negro; he is young; he had pulmonary symptoms; the preauricular nodes were enlarged; systemic reaction was very slight; the albumin/globulin ratio was reversed; the x-ray report is in keeping with this diagnosis. I wonder if we might have the x-rays demonstrated now.

DR. DAVID SHAPIRO (Chief of X-ray): As is well demonstrated, the x-ray films show enlargement of the hilar nodes and also reticulation and nodulation of the lung parenchyma. There is a stringy appearance extending from the hilum into the lung on each side. There are no visible lesions in the phalangeal bones. At one institution where we were especially interested in the bone changes in sarcoidosis, we had only one patient, in our entire series of twenty cases, with bone lesions. Even in that patient, the changes were none too typical. I believe lesions in the bones of the hands are rare. As a rule, the x-ray changes in Boeck's sarcoid are some 10 per cent with definite lesions in the bones. As a rule, the x-ray changes in Boeck's sarcoid are form to one of three types: (1) reticulation and nodulation of the lungs; (2) enlargement of the hilar or right paratracheal nodes; or (3) a combination of the lymphadenopathy and pulmonary

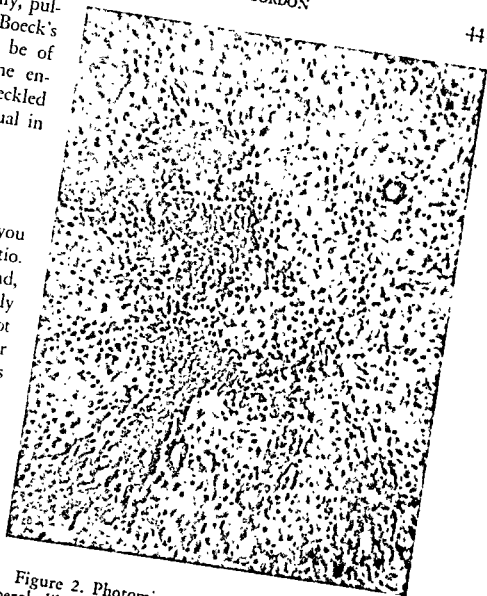


Figure 2. Photomicrograph showing numerous tubercle-like lesions with marked proliferation of monocytes and multinucleate giant cell reaction. At the periphery are groups of lymphocytes about salivary gland ducts. Caseation necrosis is absent and there is no "palisading," such as is commonly observed in frank tuberculosis.

lesions. The lesions often clear up and usually, if the patients are followed long enough, you will find old fibrosis.

DR. CORR (Chief of Medicine): As a matter of interest, I'd like to ask Dr. Kinsman how many cases of sarcoid disease he has seen. In my own experience, both in private practice and at the General Hospital in this city, sarcoidosis is not a common disease. I have seen some 6 or 7 patients who were suspected of having Boeck's sarcoid, but this is the first patient where the diagnosis was proved. Interestingly enough, while this man was still in the hospital, we received two other patients with sarcoidosis. One of these developed tuberculosis.



Figure 1. P-A film showing bilateral hilar adenopathy with nodular reticulation in both lungs. There is also some infiltration in both mid-lung fields, extending from the hilum on each side, more marked on the right.

think of, but finally we come to the disease which I think this man had—Boeck's sarcoid, or sarcoidosis. As most of you know, this is a disease so closely allied to tuberculosis that many pathologists and clinicians believe it is a form of tuberculosis. It may involve almost any organ. Recently I saw an autopsy report in which lesions were found in the spleen, lungs, lymph nodes, skin, bones, liver, heart, and intestines. The skin is said to be affected in about 50 per cent of all cases. As far as the lymph nodes are concerned, the disease has a special predilection for the pre- and postauricular

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EXPERIMENTAL

Topical Treatment With Thephorin

BEDFORD SHELMIER*

SOUTHWESTERN MEDICAL COLLEGE, DALLAS

CASE MATERIAL AND RESULTS

Thephorin Ointment was employed in 455 cases with a variety of dermatoses, but this paper describes our clinical experience in only 305 of these patients, the balance of 150 not having been observed over a sufficiently long period to warrant inclusion in this report.

Two hundred and seventy-one of the 305 cases presented were above the age of 16 years and among the children there were 14 under the age of one year.

The patients were instructed to apply the ointment as frequently as desired and in the case of infants the mothers were told to administer the salve as often as the relief obtained seemed to wear off.

As shown in Table 1, which groups together cases with identical diagnoses and summarizes the results obtained, a total of 233 patients or 76.4 per cent showed benefit from the application of the salve and 72 or 23.6 per cent were not or only slightly improved. The relief observed in the former group was classified as good to excellent in 190 cases or 62.3 per cent, and as fair in 43 or 14.1 per cent.

It can be further seen from Table 1 that atopic dermatitis, contact dermatitis, circumscribed neurodermatitis, and miscellaneous pruritic dermatoses were represented by significant numbers. Of the 29 patients with a diagnosis of atopic dermatitis, 18 or 62.1 per cent were improved from Thephorin Ointment (16 or 55.2 per cent obtained good to excellent results and 2 or 6.9 per cent fair relief).

THE discovery by Wenner and Plati of the pyridindene derivatives, a new class of compounds with specific antihistaminic action,^{1,2} added to the array of histamine antagonists a drug—2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene—whose hydrogen tartrate (phenindamine) proved effective by the oral route in combating allergic manifestations,^{3,4} and whose toxicity was shown to be distinctly lower than that of the antihistaminic drugs previously established in therapeutics and which are derivatives of ethanolamine and of ethylenediamine respectively.⁵

Any drug which is distinguished by clinical efficacy and good tolerability deserves consideration in different application forms. Therefore, it was decided to evaluate in various cutaneous disorders ointment preparations containing salts of the phenindamine base.

Two products were used: one containing as active ingredient 5 per cent of the hydrogen tartrate of the phenindamine base in "Carbowax 1500" and the other 5 per cent of the phosphate of that base in the same vehicle. Since for all practical purposes, both salts are of the same activity and of the same tolerance, no distinction will be made in recording results. For the sake of simplicity both preparations will be referred to henceforth as Thephorin Ointment.

*Department of Dermatology, Southwestern Medical College, Dallas, Texas.

¹Thephorin is the "Roche" brand of phenindamine. Liberal supplies of the Thephorin Ointment preparations were made available through the courtesy of Hoffmann-La Roche, Inc.



BEDFORD SHELMIRE

Of the 57 patients with a diagnosis of contact dermatitis, 39 or 68.4 per cent responded favorably to treatment (33 or 57.9 per cent had good to excellent results and 6 or 10.5 per cent fair results). Of the 56 patients with circumscribed neurodermatitis, 51 or 91.1 per cent were improved, with results being classified as good to excellent in 42 or 75 per cent and fair in 9 or 16.1 per cent. Of the 154 patients grouped together under miscellaneous pruritic dermatoses, 118 or 76.6 per cent derived benefit from the salve with results being good to excellent in 93 or 60.4 per cent and fair in 25 or 16.2 per cent. Obviously, the calculated percentage of success in the cases suffering from pruritus ani and pruritus vulvae have limited significance because of the small number of patients studied.

Of the lesions grouped together under miscellaneous pruritic dermatoses, 48 had been diagnosed as lichenified eczema. In 31 of these the administration of Thephorin Ointment was attended by good to excellent results and in 6 by fair results, an incidence of success of 77.1 per cent.

Of the 305 cases presented, 139 patients had suffered from their lesions for six months or longer. As appears from Table 2, 93 or 66.9 per cent of

these 139 patients obtained good to excellent results, and 18 or 13 per cent fair results with Thephorin Ointment. It can be concluded that the incidence of success in patients with chronic lesions was at least as great as in patients whose illness was of short duration only. It is worthy of note that there were 8 patients, each of whom suffered for twenty years, one for over twenty-five years, one for thirty years, one for thirty-five years, and one for over sixty years. In all of these, fair to excellent results were obtained.

CONTROLS

FIFTY control tests were performed to determine the antipruritic value of the carbowax base alone. Many of the individuals thus tested claimed to obtain moderate relief of their pruritus from the nonmedicated base. However, when Thephorin Ointment and the placebo medication were used alternately the patients invariably stated that far greater and more lasting relief of the pruritus was obtained from the salve containing Thephorin.

SKIN SENSITIZING INDEX

Of the 305 patients included in this review, one developed a sensitization dermatitis from the use of Thephorin. However, the skin sensitizing index of the ointment is somewhat higher than would appear from these figures since an additional 5 cases of contact dermatitis due to Thephorin were encountered among the 150 patients receiving the salve, but who are not included in this report. Thus there were observed 6 instances of contact-type sensitization among 455 persons, an incidence of 1.31 per cent. This is a low sensitizing index, particularly if one considers that the ointment was used by a great number of patients over a comparatively long period of time and that the quantities of the salve applied were often quite considerable. Thus of the 305 cases constituting this report 222 employed the ointment longer than one week. Several patients used the salve over the entire body. Similarly, in three infants, the whole body was covered with Thephorin Ointment (for one baby this was done 10 to 15 times during twenty-four-hour periods, with a total of 18 ounces being applied; for the second this was done 8 to 10 times daily, and for the third several times daily). On 2 other babies 1 ounce of the salve was applied daily without any signs of sensitization.

TOPICAL TREATMENT WITH THEPHORIN: SHELSMIRE

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TABLE 1
RESULTS OF TREATMENT WITH THEPHORIN OINTMENT IN 305 PATIENTS

DIAGNOSIS	TOTAL NUMBER OF CASES	RESULTS				INCIDENCE OF SUCCESS, PER CENT
		GOOD TO EXCELLENT	FAIR	POOR OR NEGATIVE	TOTAL NUMBER IMPROVED	
Atopic dermatitis (neurodermatitis, infantile allergic eczema)	29	16	2	11	18	62.1
Contact dermatitis	57	33	6	18	39	68.4
Circumscribed neurodermatitis	56	42	9	5	51	91.1
Pruritus ani, pruritus vulvae	9	6	1	2	7	77.8
Miscellaneous pruritic dermatoses	154	93	25	36	118	76.6
TOTAL	305	190	43	72	233	76.4

TABLE 2
DURATION OF ILLNESS OF 139 PATIENTS TREATED WITH THEPHORIN OINTMENT AND RESULTS OBTAINED

DURATION OF ILLNESS	TOTAL NUMBER OF CASES	RESULTS				INCIDENCE OF SUCCESS, PER CENT
		GOOD TO EXCELLENT	FAIR	POOR OR NEGATIVE	TOTAL NUMBER IMPROVED	
Six months to one year	33	21	4	8	25	75.7
One to five years	67	45	6	16	51	76.1
Five to ten years	16	9	5	2	14	87.5
More than ten years	23	18	3	2	21	91.3
TOTAL	139	93	18	28	111	79.8

OTHER SIDE EFFECTS

It was observed early in the course of this work that the application of Thephorin Ointment was attended by marked stinging and burning, without relief of itching, in cases of vesicular or oozing dermatitis and in patients whose lesions were characterized by raw sites. The use of Thephorin Ointment is therefore contraindicated in cases of acute dermatitis. In other types of dermatitis a mild stinging or burning ensues immediately after application of the salve. Many persons welcome a mild temporary stinging sensation in place of the sometimes intolerable pruritus. Several of the patients encountered this reaction only at initiation of treatment. On the other hand, in five instances the burning or stinging sensation of the skin was sufficiently severe to warrant discontinuance of Thephorin Ointment. Similarly, in 3 of the subjects complaining of burning or stinging of the eyelids, the medication had to be discontinued. In one infant the application of Thephorin Ointment over the entire body was said to have been followed by insomnia and a mild diarrhea. However, the ointment had been used for eight weeks before these symptoms developed.

Since the base, Carbowax, dissolves nail lacquer to some extent, females using the ointment should be advised of this.

DISCUSSION

OTHER workers have reported on the usefulness of another antihistaminic drug, Pyribenzamine, by topical application. For instance, Feinberg and Bernstein⁶ treated 33 cases of atopic dermatitis with 2 per cent Pyribenzamine ointment. Twenty-four of these patients reported consistent relief from the use of the salve, although some of the subjects obtained more complete relief by the simultaneous internal and local administration of the drug. Furthermore, these investigators reported 9 subjects with pruritus ani of whom 8 had symptomatic relief. Of 10 patients with miscellaneous dermatoses, 6 obtained improvement of the itching. In summarizing their results the authors state that Pyribenzamine ointment "has been found to give relief to the majority of patients with itching dermatoses, particularly atopic dermatitis and pruritus ani."

Sulzberger and his associates⁷ made a critical

survey of 90 patients treated with 2 per cent and 5 per cent Pyribenzamine cream. Of 40 cases of atopic dermatitis, 2 showed transitory improvement of the pruritus; 25 showed no change, and 13 were made worse. Of 18 cases of contact dermatitis, 2 showed definite improvement in pruritus and clinical course; 2 showed transitory improvement, and 14 showed no change or were made worse. Of 16 cases of circumscribed neurodermatitis, 8 showed definite improvement in pruritus and clinical course; 4 showed transitory improvement in pruritus and clinical course, and 4 showed no change or were made worse. Of 5 cases of pruritus ani or vulvae, 2 showed transient improvement in pruritus and 3 were unchanged or made worse. Of 11 cases of miscellaneous dermatoses, 2 showed transient improvement in pruritus and 9 cases were unchanged or made worse. Of the 90 cases using the ointment, 2 developed eczematous contact-type sensitization to the drug.

In appraising their findings, Sulzberger and his collaborators state that Pyribenzamine cream is a clean adjunct in the treatment of circumscribed neurodermatitis, but that "its value in the other dermatoses treated is questionable."

Thus, these two groups of investigators report contradictory findings. In our experience, Pyribenzamine ointment has been found of very doubtful value in the control of pruritus with results roughly paralleling those reported by Sulzberger and his associates. In contrast, Thephorin Ointment exhibited distinct antipruritic properties in a variety of dermatoses. In fact, in the majority of cases, a single application of the salve gave complete relief of the pruritus for many hours. If the itching is thus controlled, further traumatization of the lesion from scratching is prevented.

The effect of Thephorin Ointment was found to be more lasting than that afforded by preparations containing a local anesthetic and the danger of causing contact-type sensitization is not so great.

However, as pointed out, the application of Thephorin Ointment is contraindicated in all cases of vesicular and oozing dermatoses. Generally, ointment preparations possess little value in the treatment of lesions of this type, being obtained chiefly with wet dressings and lotions.

SUMMARY AND CONCLUSIONS

OINTMENT preparations, containing as ingredients 5 per cent of the hydrochloride of the antihistamine and the phosphate, respectively, of the Thephorin base, were evaluated clinically in 305 patients suffering from a variety of pruritic dermatoses. Details of the results in the various dermatoses are presented in tabulated form. Of these patients, 62.3 per cent were helped, with 62.3 per cent of good to excellent results from the salve. Thephorin Ointment is of no value in acute dermatitis, particularly in acute vesicular and oozing dermatoses. However, when such eruptions become dry and thickened, the preparation is excellent for relieving itching. It is a superior product in the treatment of neurodermatitis and of value in a high percentage of cases of atopic dermatitis. Also, in miscellaneous pruritic dermatoses, it frequently gives relief where other applications have failed.

The beneficial effects of Thephorin Ointment were at least as great in patients with lesions of several years' duration as they were in patients whose illness was of short duration only. The sensitizing index of the salve was found to be low, particularly if one considers that it was applied in many cases over a prolonged period and that frequently, large quantities were applied.

The reports of other investigators who have compared the effects of Pyribenzamine ointment with those of Thephorin Ointment in the treatment of dermatoses are discussed. In our experience, Thephorin Ointment is, by far, the superior agent for the relief of pruritic dermatoses.

REFERENCES

1. LEHMANN, G., HAGAN, E., BARBAROW, G., and ROE, M.: The antihistamine action of pyridindene derivatives. *Federation Proc.* 6: No. 1 (March) 1947.
2. LEHMANN, G.: Pharmacological properties of a new antihistaminic, 2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene (Thephorin) and derivatives. *J. Pharmacol. & Exper. Therap.* 92:249-259 (March) 1948.
3. REYNOLDS, J. L., and HORTON, B. T.: Clinical observations on the use of Thephorin (NU-1504): a new antihistaminic agent. *Proc. Staff Meet., Mayo Clin.* 22:574-577 (December) 1947.
4. PETERS, J.: Thephorin a new antihistaminic. *Illinois State J. Med.* 93:314-318 (June) 1948.
5. BOYD, L. J., WEISSBERG, J., and MCGAVACK, T. H.: Studies of the antihistamine drug Thephorin. *N. Y. State J. Med.* 48:1596-1598 (July) 1948.
6. FEINBERG, S. M., and BERNSTEIN, T. B.: Triphenylamine "Pyribenzamine" ointment for the relief of itching. *J. Invest. Dermatol.* 134:874 (July 5) 1947.
7. SULZBERGER, M. B., BAER, R. L., and LEVIN, H.: Therapy with Pyribenzamine hydrochloride. *J. Invest. Dermatol.* 10:41-42 (February) 1948.

SCIENTIFIC EXHIBIT

Diagnosis of Prostatic Disease

ROGER W. BARNES, M.D., R. THEODORE BERGMAN, M.D.,
AND D. S. RAUSTEN, M.D.

COLLEGE OF MEDICAL EVANGELISTS, LOS ANGELES

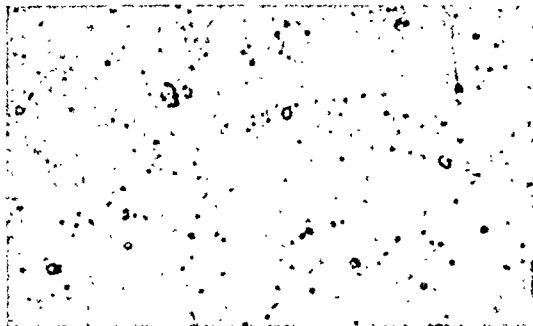


NORMAL PROSTATE

Prostatic acini lined by pseudostratified columnar epithelium, with no definite basement membrane but resting on a stroma of connective tissue, elastic tissue and smooth muscle.

NORMAL PROSTATIC FLUID

Showing lipoid granules, spermatazoa and prostatic epithelial cells.



CHARACTERISTICS OF CHRONIC CONGESTION OF THE PROSTATE



Chronic Congestion: The acini are distended with prostatic fluid so that the epithelium is flattened and the stroma compressed.

Occurrence

Very frequent
Any age after puberty

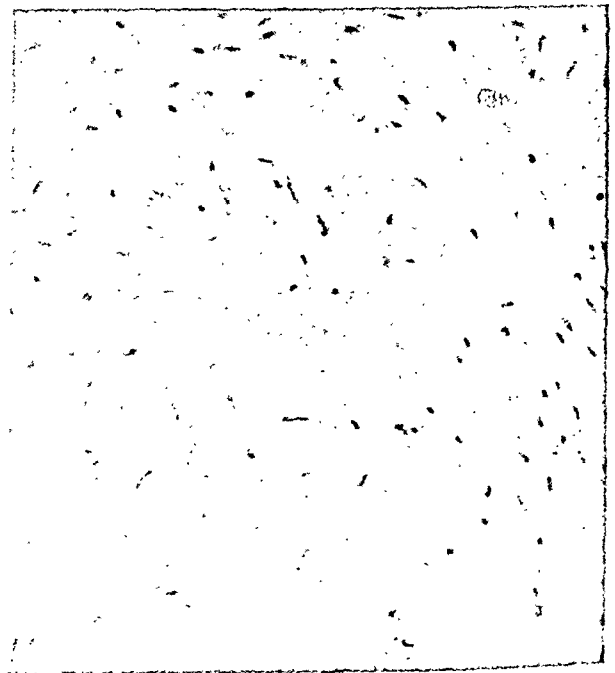
Symptoms

Heaviness or aching in perineum and rectum
Slight colorless urethral discharge more marked during constipated bowel movement
General malaise

Findings

Prostate somewhat larger than normal, soft and boggy
Seminal vesicles may be palpable, large and soft
More than a few drops of prostatic fluid obtained by gentle massage

CHARACTERISTICS OF FIBROTIC PROSTATE



Occurrence

Less common than benign hypertrophy
Any age. May be congenital; may follow long continued chronic prostatitis

Symptoms

Slowness of urinary stream
Sometimes frequency and burning on urination

Findings

Prostate small, firm, well defined and movable
Obstruction at bladder neck
May be residual urine

Fibrotic Prostate: Showing excessive fibrosis.

CHARACTERISTICS OF ACUTE PROSTATITIS

Occurrence

Any age, more common in young men
Frequently due to gonococcal infection

Symptoms

Fever
Severe pain in rectum and perineum
Difficulty voiding

Findings

Prostate large, tense, smooth, very tender
Elevation of temperature and white count
Sometimes urinary retention (avoid catheterization if possible)



Acute Prostatitis: Showing numerous polymorphonuclear leukocytes.

CHARACTERISTICS OF PROSTATIC ABSCESS

Occurrence

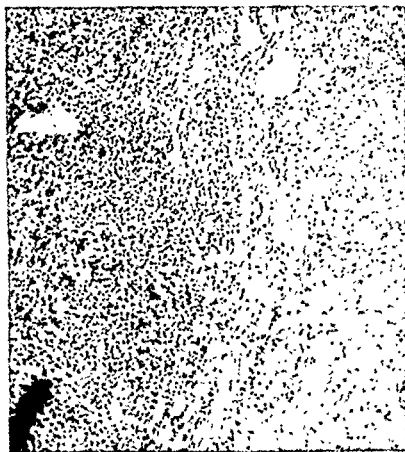
Any age, more frequent in youth and middle age
Often follows acute or subacute prostatitis

Symptoms

Dull aching pain in rectum and perineum
Frequency and pain at end of urination
Sometimes slow stream
General malaise

Findings

Fluctuating area on prostate if abscess near rectal surface
Areas of induration in remainder of prostate
P.M. elevation of temperature
May be residual urine



Prostatic Abscess: Part of necrosis shown at left with increased polymorphonuclear leukocytes and adjacent fibrosis to the right.

CHARACTERISTICS OF SUBACUTE PROSTATITIS



Subacute Prostatitis: Showing predominance of lymphocytes.

Occurrence

Any age. Rare before puberty
Often follows acute prostatitis

Symptoms

Aching pain in perineum and rectum
Frequency and burning on urination
Sometimes slow stream

Findings

Prostate somewhat enlarged, irregular, with soft areas between areas of induration; tender and may not be well defined (when there is peri-prostatitis) difficult to differentiate from carcinoma of the prostate
May be slight P.M. elevation of temperature

CHARACTERISTICS OF CHRONIC PROSTATITIS

Occurrence

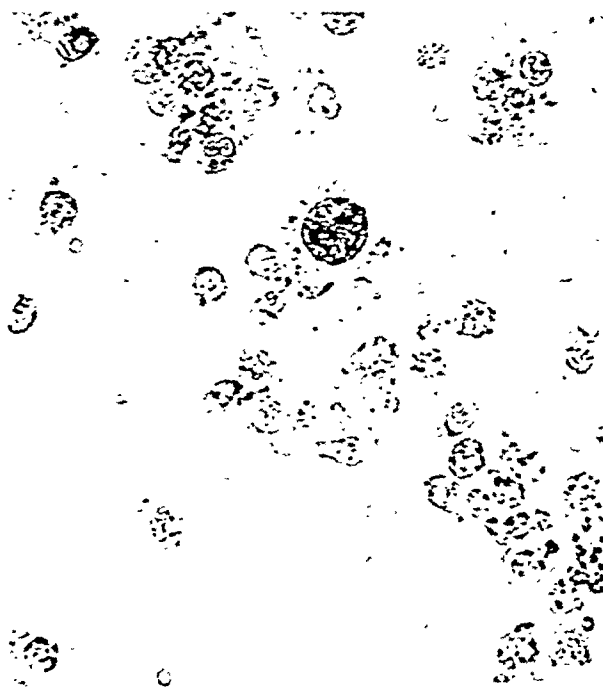
Any age. Rare before puberty
Very common
May accompany benign hypertrophy, prostatic calculi, or chronic congestion
More often nonspecific than gonococcal

Symptoms

May be none
Slight frequency and burning at end of urination
Focus of infection causing iritis, arthritis, etc.

Findings

Prostate slightly irregular, small areas of inflammatory induration
Prostatic fluid contains more than five pus cells per high-dry field



Chronic Prostatitis: Prostatic fluid from chronic prostatitis showing fifteen to twenty pus cells per high-dry field.

CHARACTERISTICS OF TUBERCULOUS PROSTATITIS

Occurrence

Usually in youth and middle age
Comparatively rare

Symptoms

Slight dull aching in perineum
Frequency and burning on urination
Usually accompanied by tuberculous cystitis

Findings

Prostate irregular; small areas of induration; one or both seminal vesicles indurated
Often accompanied by tuberculous epididymitis
Prostatic fluid may contain pus (prostatic massage is contraindicated)



Tuberculous Prostatitis: Showing from left to right (a) caseation-necrosis; (b) surrounded by area predominating in epithelioid cells, and (c) prostatic acini.

CHARACTERISTICS OF PROSTATIC CALCULI



Prostatic Calculi: Roentgenogram showing several small prostatic calculi above symphysis pubis.

Occurrence

Any age
Frequently accompanies chronic prostatitis
Fairly common, but often not diagnosed

Symptoms

May be none
Same symptoms as chronic prostatitis

Findings

May be none
Same findings as chronic prostatitis
May palpate calculi in prostate

CHARACTERISTICS OF BENIGN HYPERTROPHY



Benign Prostatic Hypertrophy: Showing hyperplasia of glandular epithelium lining the acini and forming finger-like projections into the lumen.

Occurrence

Age—usually after fifty years of age
Very common

Symptoms

Difficulty voiding
Frequency and painful urination

Findings

Prostate enlarged, smooth, regular and elastic in consistency
Obstruction at bladder neck and residual urine
May be infection and upper urinary tract damage

CHARACTERISTICS OF CARCINOMA OF THE PROSTATE

Occurrence

Age—usually about fifty years of age
About 20 per cent of men over 50 who have prostatic symptoms

Symptoms

Early—none
Late—difficulty voiding. Frequency and burning. Difficulty holding the urine. Pain in rectum, perineum and low back. Cachexia

Findings

Early—may be none. Small hard nodule palpable in capsule.
Late—prostate stony hard, fixed, usually irregular and not well defined. Obstruction in prostatic urethra and residual urine



Prostatic Adenocarcinoma: Grade II, showing an increased number of acini with irregular staining characteristics of the nuclei.



The Medical Bookman

GLOMERULAR NEPHRITIS: DIAGNOSIS AND TREATMENT*

THIS book is dedicated to "the patients, dietitians, medical students, and doctors who have worked in the Nephritis Clinic of the Outpatient Department of Stanford University Medical School in San Francisco. Here they will find a record of their observations and of the controversies in which they have taken part over many years."

The "reason" for writing this volume which the author says is "not a textbook" was due to his dissatisfaction with present-day treatment of patients with renal diseases which he states is "inadequate and sometimes dangerous."

The kidneys do an enormous amount of work, and they seem not to have the brief intervals of "rest" which the heart enjoys. Undesirable products of decomposition and "poisons" constantly require extraction from the blood. The selection of such material has always been a matter of wonder, at least to this reviewer. How does the kidney "know" what to do with the vast amount of fluids and solids which in twenty-four hours amounts to 180,000 cc.? This is 600 times larger than the kidneys themselves (page 225), and 3 times larger than the man himself. The usual measured volume obtained from urination in twenty-four hours is about 2,000 cc. Therefore, not all of the grist which comes to the mill is cast off as waste.

While much, perhaps most, of the body debris—animal, vegetable and mineral—goes through the kidneys without destroying the renal cells, there may come a time when these important organs cannot throw off certain substances, bacteria, for example. These may remain as irritants and eventually impair or destroy the cells which are in-

capable of rejecting the invader. We then have the beginning of "kidney disease," chief of which, according to Dr. Addis, is glomerular nephritis.

The clinician is concerned chiefly with the presence of albumin, casts and sugar. This author uses the term "proteinuria" in preference to albuminuria since it is the "deleterious effect of protein undernutrition" which must be watched for and be circumvented, if at all possible. "Glomerular nephritis is the only disease of the kidneys which we understand well enough to treat scientifically." However, there are limitations in the treatment of outpatients which do not obtain under hospital regimen. A patient whose economic status precludes rest periods as part of the treatment poses a difficult problem to his general medical adviser who must contrive ways and means to keep him going. Laboratory tests are expensive in the determination of creatinine, urea, and protein in the blood because frequent repetition is essential. Therefore, the office nurse must be trained in at least some of these diagnostic techniques. The "team" then consists of the patient and the doctor and the nurse" or whoever can take up the routine burden of the clinical chemistry. Efficiency is dependent upon such a team. "The growth of efficiency in medical practice is based on team work both in and out of the hospital."

The course of glomerular nephritis may be divided into four stages: the initial, the latent, the degenerative and the terminal. Unfortunately, the terminal is merely a question of time. Days, months or even years may supervene while the patient is kept fairly comfortable, and at his daily tasks. This requires medical management of a high order, and an unremitting effort to maintain the cooperation of the patient.

During the initial stage patients often comment

*Glomerular Nephritis: Diagnosis and Treatment. By Thomas Addis, M.D., F.R.C.P. (Edin.). 338 pages, illustrated. With appendix, reference table and index. New York, The Macmillan Company, 1948. Price \$8.00.

that their urine "looks like coffee." Blood comes down a long way through the tubules and is turned brown by the acidity of the fluid in which the blood cells float. Edema about the eyelids is often noteworthy, especially in the morning. It is subcutaneous, not deep in extent. Hypertension usually accompanies the degenerative or terminal stages, but it may be also an early symptom. A rising diastolic blood pressure in children may be associated with edema of the brain and resultant convulsions. The daily blood pressure may plot an interesting curve.

Dr. Addis states that all urine protein is plasma protein, and that it does not come from the disintegration of kidney cells.

Casts are important, and a careful microscopic examination of them may help to determine the location in the kidneys where they are formed. The casts are chiefly hyaline or epithelial, but blood casts are also found. The hyaline casts dissolve in water, but the blood and epithelial ones do not. The three important things about casts are: (1) where they are formed (what part of the kidney); (2) the material from which they are made; and (3) the changes which they undergo from the time of their discharge to the moment of examination under the microscope. The breadth of the cast may determine whether it has been formed in the nephron or in the tubules of Bellini. Casts which are 5 or 6 times broader than ordinary come from well down in the collecting tubules. Narrow casts come from swollen cells lining the tubules.

The extent of the lesion is best determined by ascertaining the concentration of creatinine in the serum. The rate of creatinine excretion remains constant no matter what the size of the kidney. "... a simple equation will tell us, from the serum creatinine concentration alone, the extent of any renal lesion in terms of percentage of the normal amount of renal tissue" remaining. (Page 116.)

Bacterial causes of nephritis are set down as *Strep. viridans*, *Strep. hemolyticus*, *B. typhosus*, etc. It is surprising to learn that only one per cent of scarlet fever patients develop glomerular nephritis. Table 34, page 180 cites infectious diseases preceding the initial stage of glomerular nephritis as: tonsillitis 39 per cent; scarlet fever 16 per cent; sinusitis and middle ear disease from 11 to 12 per

cent; undiagnosed infections 3 per cent. These percentages are based on a study of 115 patients.

The prognosis depends somewhat on the "theory of rest from osmotic work." It is possible to reduce the size of a kidney by manipulation of the protein intake, and appraised by protein catabolism estimation. Tables and diagrams are given to show how this may be accomplished. Conservatism in prognosis should be the watchword in every case. Under careful management, uremia may be reduced to a minimum and the patient may work in remarkable comfort for a long time. In the terminal stage, the blood urea concentration rises, the urine is more dilute, the anemia worsens, and dietetic regimen fails to bring relief.

TOWARD the end of the book a full case history of a boy is given. He developed glomerular nephritis when about 10 years old, but through careful management he was able to go through high school, college and on to postgraduate work. He became a teacher of physics and mathematics and secured a Ph.D. as a reward for his industry. Nevertheless the course of the disease was slowly progressive. The precise age at exitus is not told, but he was over 25, which means that he was assisted to maintain fair health for over fifteen years. The question may arise whether one should encourage such intellectual effort despite the limited life expectancy. The answer would seem to be about the same for all "chronics"; namely that anything which contributes to their enjoyment of life, any amusement or hobby or actual productive work which does not militate against the basic principles of therapy, is permissible. In the reported case, the patient was not told of the "fears" of his doctor, but was encouraged to carry on under common sense guidance afforded by dietetic and hygienic factors. Apparently the patient was not of the worrisome sort. He accepted his fate philosophically with a sort of "inner knowledge" of his actual condition, as is usual with astute patients. Indeed an excellent attitude for any human, facing his end. "It is the quiet drowsiness we want. The disease itself will soon bring the deep sleep." Thus ends the book.

I. W. V.

New Books Received

INTRACRANIAL TUMORS, by Percival Bailey. 2nd Edition, 478 pages, 155 illustrations; 16 plates. 1948, Charles C Thomas, Springfield, Ill. Price \$10.50.

This work on intracranial tumors comprises one of the most systematic and clearly presented treatises ever written on this subject. Dr. Bailey set out to write a book that would be read by students and physicians and in this goal he has admirably succeeded. The simplicity with which the author has succeeded in presenting this relatively complicated subject is quite unbelievable. Actually, the title of this book, namely, "Intracranial Tumors," is a little modest. Dr. Bailey has subtly interwoven in his presentation a fairly adequate discussion of neurophysiology and clinical neurology.

The first three chapters of this book are devoted to a general discussion of a "few" fundamental anatomic and physiologic concepts, including such subjects as arterial and venous supply of the brain, cerebral cytoarchitectonics, cerebrospinal fluid flow and the ventricular systems, cortical representation, etc. These chapters are followed by a separate discussion of the more common intracranial neoplasms.

The method chosen by the author for his discussion is a little unusual in text but certainly makes for added interest. Each tumor type is introduced by one or two case histories presented as if a clinic were being given. These cases are used as an introduction to a more detailed discussion of the clinical and pathologic aspects of the individual tumor types. All descriptions and discussions have been kept simple, brief but complete in every respect. Operative techniques have been reduced to a minimum and concentrated in a single small chapter at the end of the book.

The illustrations are a little unusual. In order to avoid the glare of most photographs, the author has used drawings to illustrate the entire book. At first one may be a little disappointed in these illustrations but further study of them makes one feel more and more satisfied with them.

It is indeed unusual to have such a wealth of material presented in such a charming manner by such a real authority on this subject. This book can be highly recommended to everyone in the profession as an example of excellency in medical writing. It can be particularly recommended to every student in the neurologic sciences as a "must" in his reading and an invaluable addition to his library.

A. B. B.

A-B-C'S OF SULFONAMIDE AND ANTIBIOTIC THERAPY, by Perrin H. Long, M.D., F.R.C.P., Professor of Preventive Medicine, Johns Hopkins University School of Medicine; Physician, The Johns Hopkins Hospital. 231 pages. Philadelphia and London: W. B. Saunders Company, 1948. Price \$3.50.

This book has been planned to provide concise, up-to-date information concerning the practical aspects of the use of sulfonamides and antibiotics in the treatment of infectious processes. The data is arranged in readily available form and should be of value to practitioners of medicine and surgery. The clinical pharmacology, toxicity, and methods of administration of the agents are discussed, as well as other general aids to the employment of sulfonamides and antibiotics. The author states that he has omitted a discussion of the topical use of sulfonamides and antibiotics because of the opinion and, in some cases, even harmful.

RONALD ROSS, Discoverer and Creator, by R. L. Megroz. 282 pages. 1948, George Allen and Unwin, Ltd., London and The Macmillan Company, New York. Price \$3.00.

This biographical study, first published in 1931, offers a definitive picture of a man who has distinguished himself in such apparently divergent fields as medical science and literature. Sir Ronald Ross has been honored by the Nobel Prize for his discoveries in the field of tropical medicine, but that he is a man of great versatility as evidenced by his writing of novels and poetry and musical compositions is not so well known. As Osbert Sitwell writes in the preface to the book, "Nothing that Sir Ronald Ross may do now can astonish me. . . . Seldom, since the time of Wren, can there have been a man of such extraordinary diversity of genius."

DISASES OF THE EAR, NOSE, AND THROAT, by William Wallace Morrison, M.D. 1948, Appleton-Century-Crofts, Inc., New York. Price \$8.50.

Written for the undergraduate student and general practitioner, and originally published under a different title, this book has now been completely revised and reissued. The material has been handled in a clear and concise style and presents a practical and current approach to the subjects discussed. The illustrations, prepared by the author himself, are schematic in type and lend themselves well to teaching purposes.



MEN OF MEDICINE

Albert Schweitzer... "Reverence for Life"

A FRIEND of Dr. Albert Schweitzer once asked him if he were happy.

"Yes," he replied, "when I am working and getting somewhere. As an individual, I have really ceased to exist. . . . I don't know personal happiness any more."

If "working and getting somewhere" means happiness to Schweitzer, he should be blessed with a feeling of immense well-being. For it is hard to find a man, living or dead, who has worked as hard or accomplished as much as he. To many people he is "the one great man of the century"; warm praise from men like Albert Einstein has won him the title of "the great man's great man." His phenomenal accomplishments are almost unbelievable, and all over the world, people stand in awe of the tremendous intellect, driving, relentless ambition and overwhelming, humanitarian selflessness of this giant among men. Yet Schweitzer, whose influence is known and felt throughout the globe, lives in seclusion in a French Equatorial Africa hospital.

Instead of surrounding himself with the great minds of Europe and the United States, his companions are largely African natives. Instead of the association of brilliant physicians and surgeons, the surroundings of modern, well-staffed hospitals, he consults with a few white assistants and a number of black orderlies in the small confines of his African hospital. Not since 1939, when the threat of war kept him from visiting Europe, has Schweitzer made any attempt to leave Africa. But in spite of his long absence from this part of the world, his influence has not waned. If anything, popular interest in Schweitzer and his work has grown to new and larger proportions. People, everywhere, are asking "Who is this man and what has he done?"

He is an Alsatian—a tall, well-built man with a shock of graying hair and a flowing "handle bar"

mustache—whose philosophy makes him a citizen of the whole world; a physician who studied medicine for only one purpose—to alleviate the pain and suffering of the black people in Africa. He is a theologian who balks at religious dogma; a musician whose study and mastery of the organ has brought new interpretations and meaning to organ music and to the music of Bach. As a historian, he has written one of the most thorough studies of the life of Jesus ever to be undertaken, and as a contractor and carpenter, he has built an entire hospital in the African wilds. He is a writer whose words are like poetry, and he is a farmer who grows food for his patients in ground where only creeping vines and tall grasses had lived before his coming.

But beyond those things, and underlying them, he is a supreme humanitarian who has put his thoughts into action by surrendering himself and his individuality to the betterment of his fellow men. The most outstanding testimonial to that surrender is his work as a medical missionary in Africa. But it is not his African work alone that makes him great. Hundreds of other men and women have given themselves unselfishly to missionary and medical work and have never been remembered, except by a very few. Schweitzer is great because he could give himself wholeheartedly to an African hospital—as others have done—and yet never withdraw himself from the world. His immortal contributions to the fields of theology, philosophy, and music—many of them made during his medical career—are enough to bring him lasting fame. To find a man who can organize and run an African hospital, play an organ which has been reconstructed according to his own directions, write a three-volume book on the philosophy of civilization, and explore with careful scrutiny the doctrine of Paul the Apostle is to find a genius of rare talents. But even more rare is the discovery in that man of a simple and all-consuming desire to use his brilliant talents for only one purpose—the good of other men and the dedication of himself to their happiness. When

Opposite page: Dr. Albert Schweitzer and his pet antelopes at Lambréne.

such a man is found—and Schweitzer is that man—he is indeed great.

Albert Schweitzer became a physician as a result of slow and logical thinking—the kind of thought which has produced his masterpieces of philosophical and theological writing. Although he did not enter medical school until he was 30—an age when most doctors are already practicing—his decision to become a doctor was part of a life pattern which he had laid out nine years before. For at the age of 21, Schweitzer knew without question what he would do with his life.

It was in 1896, when he was home from the University of Strasburg for the Whitsun holidays, that Schweitzer, with the calm deliberation so typical of his character, mapped out his life's plan. It was founded on his solemn, unshakable conviction that he must give himself to the service of suffering humanity, an idea which had been shaping itself within his mind for many years.

The increasing awareness that he was happy while others were not was weighing heavily upon him as he considered his future on that fateful Whitsunday. As he pondered the idea, he became more and more convinced that he must pay for his good fortune. His uncompromising sense of justice told him it was not fair that he enjoy all the advantages of life, while others, less fortunate than he, lived out their lives in misery. Moved by those conscientious promptings, he made his plan.

He would give himself nine years of personal freedom—nine glorious years to spend in the fascinating perusal of his books and the soul-releasing music of his organ. When he reached 30, that period of his life would be over. It would be time to search out the work in which he could be of greatest value to his fellowmen.

That decision, made with such resolved determination in the mind of hardly more than a child, was final. There would be no changing it! But it was a secret, too, to all but Schweitzer. He carried it with him through the precious nine years, pondering, weighing, deliberating what form his "service" should take, but never disclosing to anyone that these years were the last he would spend among them. When, at the end of the nine years, he made his startling announcement, the effect was like a thunderbolt resounding through the quiet and scholarly atmospheres of Gunsbach, Strasburg, and Paris.

There is little wonder that the people who knew Schweitzer were astounded. How many men, at

the age of 30, they asked, could point to a record like the one he had already achieved? How could he sacrifice such a brilliant future?

That career to which his friends pointed with mingled pleasure and reproach had, indeed, a singularly bright beginning. Before he began the study of medicine, his erudition in the fields of music, theology, and philosophy had already been established.

SCHWEITZER's first interest was music. At pre-school age, he began to show exceptional talent at the piano and by the time he was 18, he was an organist of such distinction that his teacher, Eugene Munch, sent him to Charles Marie Widor, professor of the organ at the Conservatoire in Paris. Widor, when he heard the young boy, recognized "a musician with a mind, an imagination and unfathomable depths of feeling and an extraordinary knowledge of Bach."

At the University of Strasburg, which Schweitzer entered that autumn, he showed a far greater knowledge of Bach than most of the organists in Strasburg. In addition to his music, he began a study of organs themselves, a preoccupation which has lasted through his entire life. As one of his biographers has said, "He has given himself almost as fully to saving organs as he has to saving souls and bodies."

A travelling scholarship took him to the Sorbonne in Paris where he studied again under Widor. The master, who admitted readily that his student knew far more than he did about Bach, urged Schweitzer to write down his interpretations of the great composer. The result was his famous book on the music of Johann Sebastian Bach which was published seven years later. A completely new German version of the 450-page volume appeared in 1908, written while Schweitzer was attending medical school.

In 1905, engrossed as he was with his decision to go to Africa, he helped organize the Paris Bach Society, and the same year was appointed organist for the Bach Concerts at the Orfeo Catala at Barcelona. In his succeeding years at medical school, he never missed a rehearsal or performance of either group.

While other men might have found the study of music a full time occupation, Schweitzer regarded it as a luxury, although a beloved one. "I have a passion for music like other men's passion

for tobacco or wine," he says. And while he indulged that passion as much as he could, his real University studies were theology and philosophy.

Schweitzer's study of religion did not follow the tried-and-true pathways of the usual seminary student. He read and learned, of course, all that the course required. But orthodoxy was not for him. As in every field of study he has undertaken, Schweitzer had to prove to himself that the things he believed in were true. From his first days at the University, he always searched and struggled for the Truth.

The son of a pastor of an evangelical church in Gunsbach, Schweitzer had been a deeply religious person all his life. For that reason, it was doubly hard for him to make the studied examination of the Gospels which his desire for truth demanded. But while he knew he was dealing with questions which reached the very core of Christian faith and challenged the innermost parts of his spirit, his probing mind demanded true answers.

Chief among the questions he wanted answered was one which concerned Jesus' eschatological prediction of the immediate ending of the world. When he had read every religious commentary he could get his hands on and had gone over the Gospels in minute detail, he drew his startling conclusion. Jesus had erred! It was not easy, in view of his deep and trusting faith in the power and infallibility of Jesus, to make known the results of his study, but Truth, no matter what the price, was of greatest importance to Schweitzer.

The aspects of this revolutionary discovery and the subsequent picture of Jesus which Schweitzer painted are much too detailed to be described in so brief a space. It is enough to say that this first major contribution of Schweitzer to religious theory established him, at the age of 26, as a theologian of note.

After publishing in 1901 his first book on the subject of Jesus' error, "The Mystery of the Kingdom of God," Schweitzer began his book on the historical Jesus, attempting to present Him, not as he would appear in the present day world, but as he actually existed hundreds of years before. The book, "The Quest of the Historical Jesus," came out in English in 1910, preceded by an earlier and similar German edition, "From Riemarus to Wrede," published in 1906. According to George Seaver, one of Schweitzer's recent biographers, "Scientifically considered, 'The Quest' is the most creative reconstruction of the life of Jesus that has

ever been or, in all probability, ever can be made from the records available."*

Although the books were completed after his thirtieth birthday, his original and relentless search for Biblical truth had impressed theologians throughout Europe long before that. He was only 25 when he received his licentiate in theology (a degree superior to that of doctor at Strasburg), and soon after, he successfully passed all examinations for his ordainment.

Side by side with the stupendous job of reading, sorting, analyzing, and deducing the material for his books on the Gospel, Schweitzer was studying for his doctorate in philosophy and writing a thesis on the religious philosophy of Kant. At the age of 24, he received his degree in philosophy, and his thesis was published in book form.

AFTER finishing at the University, followed by a short period in Berlin, Schweitzer was appointed curate of the Church of St. Nicholas in Strasburg, warden of the theological college, and lecturer at the University as a member of the Faculty of Theology.

In 1903, he was appointed principal of the Theological College of St. Thomas, which was attached to the University—one of the youngest men, at 28, ever to receive the appointment. It was a position for life, promising a good salary, independence, companionship with men of intelligence and a chance for undisturbed study.

And yet, he could not accept the prospect of the full and pleasurable life before him. He had made a promise to himself—a promise to answer the strong and powerful Voice within him which demanded that a man as happy as he must pay for his good fortune.

His thirtieth birthday was only three months away before he made up his mind what his life's work would be. The decision came impulsively, the result of an article in a report of the Paris Missionary Society. The article made a plea for more workers in the French Congo, and the picture of savages living a life of tortured superstition and pain was enough for Schweitzer. The white man's exploitation of his black brother had always been a source of deep sorrow to him. Probably the article touched off an idea which had been lurking within the shadows of his mind for

*SEAVER, GEORGE: "Albert Schweitzer, the Man and His Mind."

many years. Africa! It was there he was needed; there he could do the most good!

But why medicine?

"I wanted to be a doctor that I might be able to work without having to talk," he explains. "For years, I had been giving myself out in words . . . this new form of activity I could not represent to myself as talking about the religion of love, but only as an actual putting of it into practice."

It goes without saying that once Schweitzer had made up his mind to practice medicine in Africa, he had to go all the way in his preparations. He who had never tackled anything but the theoretical, the cultural, the artistic, was put to the task of mastering the coldly scientific realm of medicine.

He began with courses in medicine, surgery, gynecology, psychiatry, bacteriology, pathological anatomy, pharmacology. He took special courses in tropical disease and started reading as much as he could about Africa itself. Yet, with such a heavy load, he continued for the first four months to lecture on Divinity at the University. And all through medical school, he preached almost every Sunday, continued to play the organ part for the Paris Bach Society and the Orfeo Catala every winter and played several other concert engagements in France and Germany. Almost unbelievably, he was also writing his "Essay on Organizing," and completing the final chapter of his "Quest." And as a crowning achievement, he completed his first work on the history of Pauline doctrine, "Paul and His Interpreters."

His last three years in medical school were less strenuous. But while he enjoyed the clinical course far more than he did the first years of medical study, he was still under a strain of fatigue and overwork. He entered for the finals of the State Medical Examinations in 1911, and while preparing for them he also undertook, with Widor, a complete edition of Bach's music which was to comprise five volumes. (The work has never been finished.)

In his last year at the hospital, he continued to work on the Bach volumes, at the same time preparing his thesis for the medical doctorate, doing practical work in the hospitals, making a special study of tropical diseases, and collecting funds for his mission.

As if the criticisms of his friends ("how much I suffered," he wrote, "through so many people assuming the right to tear open all the doors and shutters of my inner self"), and seven years at the

University were not obstacles enough to his African goal, he was faced with a third obstruction. Members of the Paris Mission, to whom he offered his services, objected to Schweitzer's "incorrect" theological position. Even if his Christian love could not be denied, they found it hard to accept a mission doctor whose Christian belief did not toe the line of mission doctrine. Not until he visited each member of the Society personally, persuading each one that he wanted to help "only as a doctor," did the Mission accept his gratuitous offer.

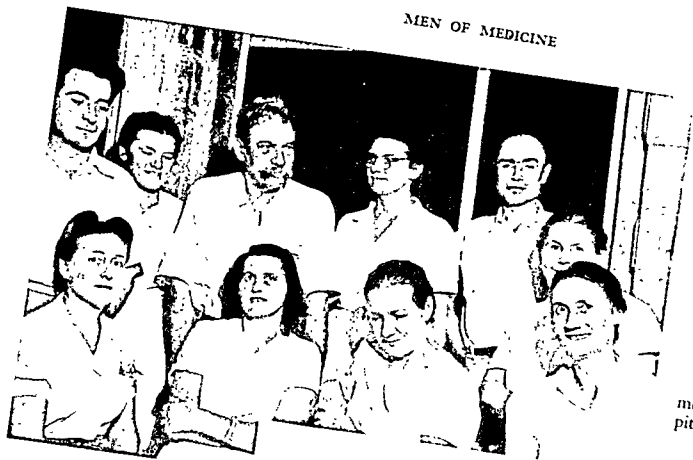
He was given permission to establish his hospital, the Society put a house at the Lamberene Mission Station at his disposal, and promised to help in furnishing labor. He, in turn, promised to pay for founding, equipping and maintaining the hospital as well as paying the expense of his own household.

Although Schweitzer's agreement with the Paris Mission appears to be somewhat one-sided, he was highly pleased. The committee gave him a free hand, reminding him only that he should not preach. But as things turned out, that prohibition was removed a few months after his arrival at the general request of his fellow missionaries.

In 1912, Schweitzer had married Helene Bresslau, a trained nurse who shared his ideas of serving mankind. With her, he set out for Lamberene on March 26, 1913, cutting himself off with a swift, sure stroke, from the European atmosphere he loved so much.

His life in Africa began, characteristically, with a disappointment. His wife and he arrived at the mouth of the Ogowe River in the middle of April, and went from there by river boat to Lamberene. When they arrived, they found no evidence of the building which had been promised by the Mission. But with his usual versatility, heightened by his anxiety to begin work at once, he soon had a hospital organized—a windowless, broken-down hen house was his surgery; his own bungalow his dispensary, and the open courtyard his clinic. There, until the regular evening rains drove them away, he treated his first patients.

The shortages which Schweitzer found in building materials, housing, food, labor, were never repeated in the number of patients who began flocking to him from distances of more than 200 miles. From the very first day, he was besieged by natives suffering from the evil diseases of the jun-



Dr. Schweitzer and members of the hospital staff.

The hospital at Lam-
beréne.



Hospital staff mem-
bers.



All photographs by
Charles R. Joy (Beacon
Press), reproduced from
the forthcoming Beacon
Press-Harper and Brothers
book, "The Africa of
Albert Schweitzer."

gle—malaria, leprosy, sleeping sickness, dysentery, tropical ulcers, elephantiasis. Among the 2,000 patients whom he treated during his first nine months, he found that hernia, pneumonia, and heart disease were also common, and that except for cancer and appendicitis, every European disease was represented among his patients.

In his writings, Schweitzer mentions the several "unmentionable" diseases he found, "each one more loathsome than the last, which have been brought to these children of nature by Europeans."

Almost as soon as he began practicing medicine, the philosopher-theologian-musician-doctor became a builder. He, who had never before built so much as a lean-to, was determined to build a hospital—if need be, with his own hands. The missionaries gave him 4,000 francs and permission to use a more favorable location—and he set to work.

A timber merchant passing by lent him his crew, but there was "something grandiose" in the laziness of the workers. Schweitzer worked along with them, for when he was gone, they would not lift a finger. The foreman of the gang would do no more than lie in the shade and speak encouragingly.

After two days of almost no work, the laborers collected their pay, headed for the nearest village, and returned to their jobs blind drunk. Schweitzer, his native orderly, Joseph, and two mechanics borrowed from the mission, were left to complete the building alone. The doctor, resenting every minute that took him away from his medical work, and hindered by his colossal ignorance of carpentry and construction, tackled the job with gusto. Before the rainy season in November, he and his assistants had completed the hospital.

The new building contained a consultation room, an operating theater, sterilization room and dispensary. There were cement floors, a roof of palm leaves held in place by slender tree stems, and high, wide windows. Almost entirely with his own hands, Schweitzer built a waiting room and a dormitory of unhewn logs and raffia leaves. For mattresses, he used dried grass.

Sometimes the work was almost too much for him, and the temper which he had inherited from his mother would break out. Because he loathes slipshod work of any kind, he insisted that his diagnoses be certain in every case. Yet how could he spend hours over his microscope when a score of natives were waiting for treatment? He had to find time, too, to prepare medicines in his phar-

macy, and acting as his own commissary, he worried about providing food for his patients. In spite of his ruling that patients bring food or they would not be treated, many of them arrived empty-handed, and his compassionate heart could not turn them away.

He was the only doctor within a radius of 100 miles. If an emergency operation had to be performed at any time of the day or night, who else could be called? He was totally responsible for saving a life or saving a man from days of torture. Could he give in to his weariness for such an enormous price?

Schweitzer's iron will has never been able to overcome his extreme sensitivity to the suffering of others. "I belong unfortunately," he says, "to the number of those medical men who have not the robust temperament which is desirable in that calling, and so are consumed with unceasing anxiety about the condition of their severe cases and of those on whom they have operated."

THE natives, who believe he can perform magic far superior to that of their witch doctors, have labeled him Oganga—"Medicine Man." But Schweitzer will not take advantage of their faith in him to spread religious dogma or doctrine. On Sunday, he preaches simple sermons to them, trying to impress upon them, as well as he can, the meaning of justice, love, forgiveness, faith in God—trying to erase, as well, the terrible cloud of superstitious fear in which they live. His missionary work, as all his work, depends only upon his belief in the simple Gospel as it was preached by Jesus in his Sermon on the Mount.

For four and one-half years, Schweitzer labored without pause in his Lamberene hospital. Although it is the custom among white people in Africa to take a vacation from the jungle every two years, neither he nor his wife returned to Europe in all that time. He allowed himself almost no recreation—with one exception. During his lunch hour and on Sunday afternoons, he permitted himself the immeasurable luxury of playing his specially constructed piano, which had been a parting gift from the Paris Bach Society.

Schweitzer had told himself that Africa would mean the end of his life as an artist, and at first he scarcely had the heart to practice. The thought occurred to him one day, however, that his precious free hours in the jungle could be used to ad-

vantage. His methodical mind at once formulated an ambitious program. One after another, he would take the compositions of the great composers of organ music, study them down to the smallest detail and learn each one by heart. His practicing, which never lasted more than a half hour a day, was to serve in good stead in later years, when he returned to Europe for concerts which financed his hospital.

WHEN war was declared in August, 1914, Schweitzer received the news with deep sadness. As German subjects, he and his wife were immediately interned in their bungalow, and refused permission to operate their hospital. The unwelcome interruption to his work was a great irritation, but the internment itself was a benefit to the doctor. Since arriving in Africa, he had been much too busy with medical work to spend any time writing. This opportunity to rest and renew his strength also awakened thoughts and ideas which had been occupying his mind since childhood. There was a book he wanted to write . . . a book which would express his pessimistic outlook on the progress of civilization.

The advent of the war only confirmed what Schweitzer had always suspected . . . that the world, instead of progressing as most people assumed, was in actuality in a state of regression. He had not been interned two days before he began his book on the decline of civilization and his prescription for its recovery. Night after night, even after resuming his medical work (he was released at the insistence of the missionaries and natives), he sat up recording with great emotion his thoughts upon the subject.

Thus began the greatest of Schweitzer's literary work, the three-volume "Philosophy of Civilization." Two volumes, "The Decay and Restoration of Civilization," and "The Civilization and Ethics of Civilization" are still in preparation. When he picked up his pen once more in 1914, it was to begin again his career as a brilliant writer. Through the years, no matter how hard he is working or how spent his energy, he has continued to devote a part of his time to thought and to writing.

The mental activity of the man is indeed fabulous . . . and it is coupled with a physical energy that is phenomenal. Now 73 years old, he still maintains a daily schedule that would normally bring a much younger man near to physical col-

lapse. From the time he arises at 6:45 A.M. until he retires at midnight or later, he does not stop to rest except for a short midday siesta. His medical work takes first precedent, but besides treating patients morning, afternoon, and evening, he is the force which holds the entire Lamberene hospital and settlement together. He is, in short, the Lamberene hospital, and one wonders what will become of it when he is no longer there.

"I surprise myself by the way I am able to carry on my work, week in and week out, without a break," Schweitzer writes. "If I went on holiday, I would find out how tired I am."

In spite of his crowded day, Schweitzer still finds time each evening for an hour's practice at his piano. And hardly a night goes by that he does not work on the third volume of his *Philosophy of Civilization*. Most of the thought which goes into that book is carried out while he goes about his daily work. "Happily, I have always had the faculty," he says, "while busy with other work of concentrating my mind on the chapter on hand." It is not out of the ordinary for Schweitzer, after he has paid his final visit to the hospital at 11:30 P.M. to work far into the early morning hours.

Thought is the basis of all existence for Schweitzer. Throughout his writings, there is a plea to every person to think for himself, to formulate his own philosophic conception of life. Mankind's "capacity for elemental thinking" is languishing, he believes.

Schweitzer has been deeply preoccupied with the great thought of the world since early University days. Since 1900, he has set himself to study, within the permits of time, all the great philosophies and religions of the world. His thirst for knowledge will never be satisfied, but the philosophical and religious writings into which he has delved are amazingly broad.

Mental work, Schweitzer says, is necessary in Africa to keep up moral health—to counteract "the terrible prose" of African life. But it is not Africa which prompts Schweitzer to think. Thought is as natural and necessary to him as breathing.

It took him fifteen years to think out the answer to the greatest question he has ever set himself to solve. And that answer has formed the basis of his entire life philosophy.

"Why am I justified," he asked himself, "in my firm belief that life is worth living? My knowledge of the world is pessimistic. Why is my viewpoint toward life optimistic?"

Since 1899, he had pondered that question with-

out being able to capture the elusive answer. There was, he felt sure, one basic thought which would give life purpose and meaning. He found that thought in his fortieth year as he traveled slowly upstream on the Ogowe River, bringing medical aid to the wife of a missionary. In typical Schweitzer fashion, he was deep in thought, for he is a man who never wastes a moment of his life. As so often before, in his never-ending search for the key to the riddle of existence, he asked himself the question, "What is it that ethics and the affirmation of life and the world have in common?" And from time to time, he scribbled words, phrases, disconnected sentences on a sheet of paper. He traveled in this manner for two days. Suddenly, at the end of the second day, the words flashed before him—clear and sharp on the whiteness of the page—"Reverence for Life!"

That was it! That was the thought which must guide men's lives!

Since that enlightening moment in 1915, Schweitzer has been convinced he has found the thought which could save civilization from its present decaying state. If man would live, Schweitzer says, by the world-and-life ethics which Reverence for Life imposes—revering himself, his fellowmen, the animals, the trees, everything that lives and grows—civilization would not face the threat of degeneration. He is optimistic in the hope that mankind can redeem itself through a constant seeking after truth. World-and-life affirmation (words which appear over and over again in all of Schweitzer's writing) contains within itself an optimistic willing and hoping which can never be lost, he believes. That belief in the value of existence is at the root of his entire philosophy.

But if Schweitzer did not find the words which expressed his philosophy until he was 40, he was practicing it long before.

"However much concerned I was at the problem of the misery in the world," he wrote, "I never let myself get lost in brooding over it; I always held firmly to the thought that each one of us can do a little to bring some portion of it to an end. Thus I came gradually to rest content in the knowledge that there is only one thing we can understand about the problem, and that is that each of us has to go his own way, but as one who means to help bring about deliverance."

Year after year, Schweitzer has gone "his own way," carrying out in practice the thoughts and ideas he has recorded in his books.

THE first break in his African career came in 1917, four years after his arrival, when he was ordered to return to a European prison camp. On the boat to France, Schweitzer was not allowed to write, but even under his depressing circumstances, he set himself to the task of memorizing some Bach fugues and one of Widor's symphonies. That relentless drive never to waste a moment of his life went with him into the prison camps which followed. At a camp at Garaison in the Pyrenees, he became camp doctor and with no books at his disposal, began questioning each of his fellow prisoners—cooks, priests, shoemakers, waiters, architects, musicians, tailors, bankers—absorbing new knowledge in fields which he had never before explored. Every day, on a plank which he marked as an organ keyboard, he memorized more Bach and Widor, pumping the notes out silently from imaginary pedals on the floor. He did not forget his Philosophy of Civilization, although he had left the original manuscript in the safekeeping of an American missionary.

From Garaison, Schweitzer, in a very weakened state, was sent with his wife to the same monastery near Arles where Van Gogh had been imprisoned before his death. And in midsummer, he was returned at last to Gunsbach, drained of his strength and sick at heart.

For the first time in his life—he was 43—Schweitzer was face to face with failure. He underwent an operation, and during the long weeks of recovery, he looked with increasing discouragement on the wreckage of his life. His hospital was in ruins, and he had no income to rebuild it, only enormous debts owed to the Missionary Society and to Paris friends. He had not even the physical strength or health to begin again, let alone support his wife or the daughter who had been born shortly after the Armistice.

He accepted two offers to serve on the staff of the municipal hospital at Strasburg and as curate of the church of St. Nicholas. But he was depressed by the sad dénouement of the dream which he had built and lost.

He believed himself to be forgotten or ignored by the world of scholarship, saying he felt "rather like a coin that has rolled under a piece of furniture and remained there lost." But he was not as forgotten as he supposed. In December, 1919, he was invited to deliver a series of lectures at the University of Upsala in Sweden for the following spring. From that time the future brightened.

At the suggestion of his friend, Archbishop Soderblom, of Sweden, he began a series of recitals and lectures in that country, and within a few weeks, he was able to remove the most pressing of his debts.

He returned to Strasburg in the summer of 1920 and wrote his first book on the "Primaeval Forest" which was translated into five languages. In 1921, he resigned both his Strasburg posts and moved to his father's home, determined to make his living from his organ and his pen. But his lectures and recitals in Sweden had put him back in the public eye, and he was much in demand. From the autumn of 1921, he was lecturing and travelling continually. He went to Switzerland and again to Sweden, made his first trip to England, journeyed to Denmark, and Czechoslovakia, Moravia and Bohemia.

His lectures were greeted everywhere with excited enthusiasm. In most countries, he lectured with an interpreter, rehearsing his speeches first in "short, simple and clearly constructed sentences." Audiences everywhere have claimed Schweitzer works so closely and in such rapport with his interpreters that his lectures are as spell-binding as if he were speaking to each audience in its native tongue.

A year before he returned to Africa, his first two volumes on the Philosophy of Civilization were completed. And that same summer, he recalls, he was also inspired with the idea for a later book, "Memoirs of Childhood and Youth."

By the close of 1923, he was preparing to return to Africa, this time without his wife whose health could not take the strain of the jungle. Accompanying him was a young Oxford medical student, Noel Gillespie, who was succeeded, in later years, by a procession of equally zestful and dedicated young men.

The chaos he found when he reached his Mission was disheartening. His hospital lay in ruins, the roofs rotted, the native-built buildings collapsed, the paths overgrown with weeds, and only a skeleton of the consulting room and pharmacy left standing. Native labor was unobtainable; the timber trade was too prosperous. But Schweitzer could not be defeated. He set out at once to search for "leaf tiles" for roofing, and acquired 64 before evening.

That was only a start. For the next eighteen months, his work of the first period was but a shadow of the labor he put forth to reconstruct his hospital.

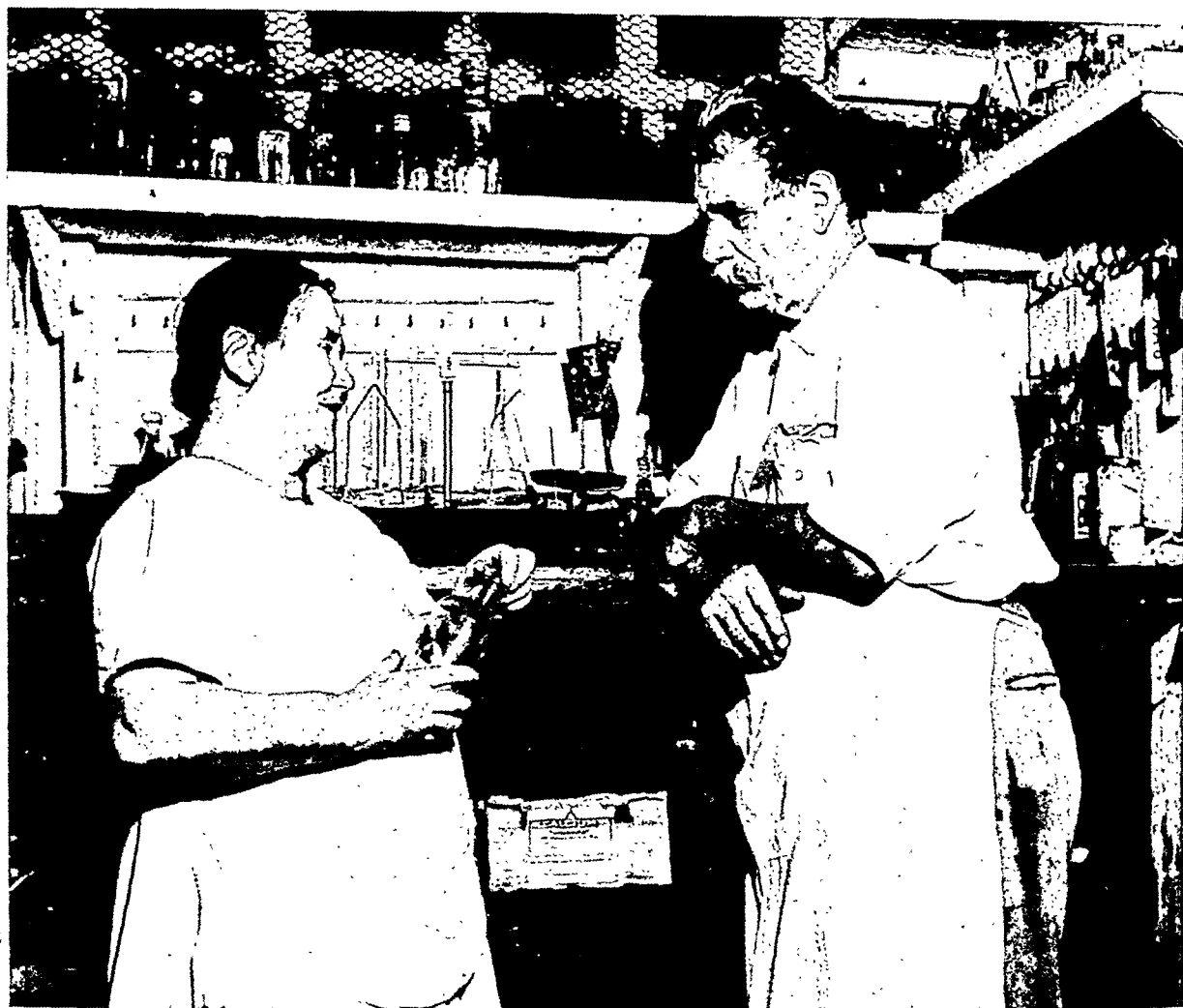
George Seaver relates in his biography, "Only a reader with imaginative insight can begin to appreciate the severity of the strain to which he subjected himself, in body and mind, during this period. . . . Only a man with such qualities as he possessed—a rugged frame and an iron will, a brain of ice and a heart of fire—could have stood such a strain without a respite during these first months."

That respite appeared in October when a doctor from Strasburg arrived to help him. Gillespie's time had already elapsed, and he had returned to Europe. The help of the young doctor, Victor Nessman, was incalculable. Ironically, it enabled the brilliant doctor to devote more time not to scientific study or writing or music, but to building. He constructed beds and bed frames (traveling as far as 60 miles for wood), a hut for storing tools, another for food, a ward accommodating 30 beds and a separate ward for surgical cases, and a house for the new doctor and for white patients.

LITTLE by little, things progressed. Another surgeon from Berne came bringing with him a nurse. More buildings to house supplies and a 10-room house on piles with a corrugated-iron roof were built under Schweitzer's direction. Friends in Sweden and in Jutland each sent him a motor boat, and a Swiss builder volunteered his services for several months.

In the meantime, the number of his patients was increasing by leaps and bounds. Their numbers became so great that Schweitzer began to recognize the need for a larger hospital in a wider area. He had boats now, and lumber given to him by a grateful patient. But still he had to shoulder all responsibility for planning the design and supervising the building—the natives would obey no one else!

Building the new hospital meant sacrificing a trip back to Europe for the construction would take at least a year. He set to work at once, pegging out the area first, and stumbling through swamps, thickets, hordes of red ants and all the other jungle impediments. The hospital had to be built on piles, since no brick or stones were obtainable, and each pile, carried 16 miles up the river, had to be charred at the end. He set and fixed each pile himself. With mathematical precision, he worked out the most suitable measurement for their width and breadth and for their numbers and distances apart. The same precision



Dr. Schweitzer and nurse in the pharmacy of the hospital at Lamberéne.

went into the measurements for wards and beds.

The hospital was built of hardwood with corrugated iron roof, and slowly it began to take shape. When it was finished, it represented a plan of design and arrangement worthy of the most well-trained contractor.

Schweitzer found time for other things—digging a well, cultivating a vegetable garden, and attending to the serious cases in the hospital. For in spite of the time-consuming work of building the hospital, his concern for his patients was never a secondary matter.

In 1927, he moved the last of his patients to the new hospital, exulting that at last his patients were housed as human beings should be.

With the final completion of the main building

and of plans for a five-room house which would “some day” house the doctors, Schweitzer was ready to return to Europe for a visit with his family. Since then, he has returned to Europe four times, from 1927-29, 1932-33, 1934-February, 1935, and September, 1935-1937. In 1939, he attempted another trip, but upon arriving in Europe, he realized that the threat of war was too near; he turned around and went back to Africa at once.

In Europe, he divided his time between lecturing, writing, and recitals to raise money to continue his work in Africa. His tours were remarkable in their scope. During his visit which began in 1927, for example, he traveled to eight countries, delivering countless lectures, sometimes as many as one or two a day for a week. In addition,

he completed his work on "The Mysticism of Paul the Apostle" and delivered an address on Goethe at Frankfurt where he received the Goethe Prize from that city.

His accomplishments in the last twenty years are too numerous to mention. "Out of My Life and Thought," his autobiography, which he wrote in Africa, was published in 1931. "More From the Primaeval Forest" came out in 1931 also, and "Indian Thought and Its Development" in 1936. In 1938, "From My African Notebook" appeared. And all this time, he has been working on his final volume of the Philosophy of Civilization. He has delivered lectures at all the outstanding universities in Europe and continued to thrill millions of listeners with the indescribable beauty of his organ music.

ONE can go at great length into the myriad things which Albert Schweitzer has done and still not capture the essence and quality of the man himself. He is human nature at its most splendid—a living example of the heights to which man, at his best, can attain. Everything about him is in accord with the greatness of his being—his broad, robust, well-built body, his massive intellect, his direct, unaffected manner. He gives the impression of invincibility—a man who knows where he wants to go and is going there, led by one, all-important desire to improve life and make it even more worth living.

In all his years, he has kept himself close to life, feeling a deep affinity for all that grows and breathes. His Reverence for Life is so profound that he will not harm the lowliest weed or the most obnoxious form of animal life—unless it is threatening the existence of other living forms. But he never escapes from reality, and while it saddens him, he is aware that Reverence for Life cannot alter the fact that life owes its existence to other life. If people and animals must eat, then growing things must die. But any waste of life—vegetable or animal—is to him appalling.

Schweitzer, despite his warm sense of humor, is a man who takes everything seriously. He is an alien to the world of superficial interests, not because he scorns it, but because he has no time for it. His friendships are a curious mixture of deep affection and reticence. He is never able to open himself entirely to anyone, yet is always willing to listen to the troubles of others. For his friends, he built a special Guest House at Gunsbach, paid

for it with the Goethe Prize money. Whether or not their host is there, guests continually throng the house, where they are made to feel completely at home.

Unlike most philosophers, who deal almost totally in abstractions, Schweitzer insists that all things be brought into the realm of reality. He is a firm believer that idealism can be applied to the everyday world. His description of Paul the Apostle could well be ascribed to him:

"Side by side with Paul's achievement as a thinker must be set his achievement as a man. . . . So long as the earthly world with all its circumstances still subsists, what we have to do is so to live in it in the spirit of unworldliness that truth and peace already make their influence felt in it. That is the ideal of Paul's ethic, to live with eyes fixed upon eternity, while standing firmly on the solid ground of reality. . . ."

The medical world will not laud Albert Schweitzer for his startling discoveries in the field of medical science. He is not in Africa to study diseases but to help the people they afflict. He welcomes new discoveries with heartfelt gratitude, but he has not the time for pioneering in scientific experimentation. His enormous contribution to medicine has been the day-to-day, steady plodding of the general practitioner, fighting against overwhelming odds which he can never wholly conquer. Yet never ceasing in his attempt to help as many as he can as much as he can.

Africa has become the symbol of his life. There he is satisfying his inner compulsion to perform the duty which life demands of him and to live life as he believes it ought to be lived. However stimulating or inspirational his writings, his life, itself, does more than anything else to show the world that life can be worth living!

Surely here is a tribute to the dignity of man!

BAYLE ZUROVSKY

Books by and about Dr. Schweitzer which the author consulted include: Schweitzer, "The Forest Hospital at Lambréne" (translated by C. T. Campeon), New York, Henry Holt and Company, 1931; "From My African Notebook" (translated by Mrs. C. E. B. Russell), London, Allen, 1938; "Memoirs of Childhood and Youth" (translated by C. T. Campeon), London, Allen, 1934; "My Life and Thought" (translated by C. T. Campeon), New York, Henry Holt and Company, 1933; "On the Edge of the Primeval Forest" (translated by C. T. Campeon), London, A. and C. Black, Ltd., 1932; Hagedorn, Hermann, "Prophet in the Wilderness," Macmillan, 1947; Joy, C. R., editor, "Albert Schweitzer: An Anthology," New York, Harper, 1947; Kraus, Oscar, "Albert Schweitzer, His Work and His Philosophy," London, Black, 1944; Seaver, George, "Albert Schweitzer, the Man and His Mind," Harper, 1947.



EDITORIALS

ALCOHOLISM

TODAY, more than ever before, medicine and psychiatry are working with the problem of alcoholism. Alcoholism is now recognized generally, in most instances, as a symptom of emotional illness—ranging from a major psychiatric reaction to an attempt to escape from dreary existence—and is definitely to be distinguished from social drinking. However, the dangers of heavy social and heavy *daytime* drinking must be more thoroughly understood.

When we describe an alcoholic as a sick person, the description is accurate. But, in common with those suffering from other illnesses, many alcoholics can be "cured." Some even work out their own recovery. Just what is an alcoholic? So far as any especial alcoholic personality type is concerned, there is none. By and large (excluding the total psychopath, the psychotic, the epileptic, the deteriorated, and the feeble-minded), the alcoholic of today has better than average intelligence but a poorly integrated personality, with marked emotional instability and inability to accept frustrations.

His unsatisfactory interpersonal relationships and emotional immaturity, which place self above all else, produce a need which he thinks can be satisfied through the use of alcohol—as a narcotic, as an anesthetic, or as a release from the bonds which tie him to a hum-drum, every-day plane of living.

But, unlike the social and even the occasionally intoxicated drinker, alcohol dominates him to the extent that it drastically affects one or more of his essential life activities, such as his ability to maintain economic equilibrium,

his reputation, or the harmony of his home life. Loss of insight, or the ability to evaluate what damage his drinking is doing to himself and others, is a usual consequence.

For any or all of these reasons the alcoholic should be recognized as a sick person who needs competent psychiatric treatment. How he got that way in the first place may be just as complicated and hard to define concretely as will be the treatment needed for his cure. Actually, an alcoholic is developed by many inter-related factors, together with his biological make-up and metabolism. He is the product of his ancestry—their racial background, drinking, and other life habits. His own personality, of course, results in part from his early experiences in life—his hurts and happiness—and also his later experiences, which may be profoundly formative. Among these are vocational factors, emotional experiences, religious attitudes and convictions, ideologies, the social drinking habits of his friends, and the social pressure to drink among friends and business associates. Then there are his own inner drives, striving against inhibitory barriers. To round out a picture of an alcoholic, insofar as that is possible, it may be said that studies of both men and women many times reveal the following characteristics: self-pampering; frustrated strong urges; a habit of avoiding responsibilities; various emotional hurts; psychosexual frustrations and hurts; and the emotional urge to take the brakes off certain sex drives and allow them free range.

Also, psychiatric study may often bring out marked insecurities constantly active in the personality, and identification and imitation factors, rather than any inherited tendency to be an alcoholic. Alcoholism may result, in

some cases, from heavy social drinking, time, body changes, and strains and griefs of life. According to some investigators, on the other hand, alcoholism may be evidence of latent or overt homosexual ingredients or of intense, unconscious, self-destructive tendencies.

To repeat, an alcoholic is a sick man, but his addiction to alcohol is itself a symptom rather than a disease. Alcoholism may be part of any psychiatric clinical reaction or produced by any psychiatric clinical reaction. It presents itself like the top of an iceberg. The great need is to understand what lies beneath. Each patient must be taken as a wholly new, and entirely different, problem.

Concerning treatment, beside the medical psychological approach, there are reports that some alcoholics have stopped drinking by themselves. Others have been helped by religious groups, lay groups, and lay-and-religious groups. Even the old "Keeley Cure" helped many an alcoholic—and some now recommend a conditioning or aversion treatment

without psychotherapy; while others, with deeper interest, use this method in order to get a beach-head on the patient and then follow up with psychotherapy. Generally speaking—deep, lengthy psychoanalysis alone, hypnosis alone, hypnoanalysis alone, narco-analysis alone, or the assaultive therapies alone—such as chemical, drug, or electric shock, or various types of lobotomy—are not helpful. In the treatment of alcoholism, competent, especially trained psychiatrists with a broad medical background are needed.

Because of alcoholism's widespread, insidious encroachment in all spheres of life, and its destructive effects on the family and on the community, the medical profession and allied sciences must attack the problem in its early stages. Moreover, they should strongly support existing community programs, educational courses, and church activities, giving to these the solidarity of medical backing and guidance to aid us in prevention of this major social health problem.

ROBERT V. SELIGER, M.D.

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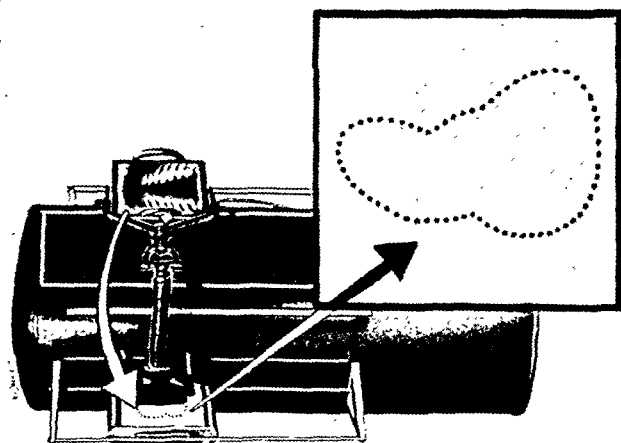
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Information published in this department has been supplied by the manufacturers of the products described.



ELECTRONIC STYLUS

PURPOSE: Attachment for fluoroscopes.

The complete unit consists of (1) bracket and guide rod assembly which mounts on fluoroscope cabinet to provide support and vertical movement guide for recording paper holder; (2) adjustable tension, writing stylus encased to mount on fluoroscope arm; (3) new screen back with lead cross for alignment of target; and (4) depression switch mounted on either right or left screen handle. Only requirement after mounting is a convenient 110 volt A.C. outlet.

The resulting image on the recording paper will not be enlarged as viewed on the screen itself but will be the true size and shape of the internal organ being traced.

PRODUCER: Continental X-ray Corporation, Chicago, Ill.

METHADON HYDROCHLORIDE

PURPOSE: An analgesic agent for relief of moderate to severe pain.

COMPOSITION: 6-Dimethylamino-4, 4-diphenyl-3-heptanone hydrochloride.

DESCRIPTION: A synthetic drug whose action resembles that of morphine in most respects, and is equal to or superior to morphine in analgesic potency.

INDICATIONS FOR USE: Recommended as an analgesic agent for relief of pain in the same conditions for which morphine, codeine, and mepheridine are indicated.

CAUTIONS: Indications and contraindications for use of the drug should be considered analogous to those of morphine until additional data permit a more comprehensive evaluation. Unlike morphine, however, methadon alone is not recommended for preoperative sedation or in the practice of obstetrics.

DOSAGE AND ADMINISTRATION: Effective adult doses range between 2.5 and 10 mg., depending on intensity of pain and

its etiology. Doses up to 15 mg. may be considered in cases of severe pain. Pain is relieved in a majority of cases by doses of 7.5 mg. orally every three or four hours. For cough, 1.25 to 2.5 mg. orally is given every three hours. For parenteral administration, the recommended dose is 2.5 to 10 mg., injected subcutaneously. Injection may be made intramuscularly if it appears desirable.

HOW SUPPLIED: Tablets of 2.5 mg., 5 mg., and 7.5 mg., bottles of 100 and 1,000. Also supplied in solution containing 10 mg. per cc., in 1-cc. size ampules, in boxes of 6 and 25.

PRODUCER: Abbott Laboratories, North Chicago, Ill.

COMPANOL

PURPOSE: For prevention of travel sickness.

COMPOSITION: Each tablet contains:

Scopolamine hydrobromide.....0.22 mg. (1/300 gr.)

Atropine sulfate.....0.16 mg. (1/400 gr.)

Luminal (brand of phenobarbital). 32 mg. (1/2 gr.)

DOSAGE AND ADMINISTRATION: Companol is administered before, at the onset of travel, and during travel. Adults should take 1 tablet thirty minutes before boarding a ship, airplane, train, or car. A second tablet is administered at the time of embarkation. Additional tablets (1 at a time) may be taken every three or four hours, if necessary. The total dose should be kept as small as possible, being limited usually to 4 tablets a day.

CAUTION: The danger of overdosage and idiosyncrasies to the components of Companol should be kept in mind. Caution is particularly indicated in prescribing Companol to pilots or automobile drivers because it may produce drowsiness.

HOW SUPPLIED: In tubes of 12 and bottles of 50 tablets.

PRODUCER: Winthrop Chemical Company, Inc., New York 13, N. Y.

TRESAMIDE TABLETS

PURPOSE: A sulfonamide triad that reduces renal crystalluria and toxic reactions.

COMPOSITION: Each 0.5 gm. Tresamide Tablet contains:

Sulfamerazine.....0.1 gm.

Sulfadiazine.....0.2 gm.

Sulfathiazole.....0.2 gm.

INDICATIONS FOR USE: Treatment of acute pneumonia, and also hemolytic streptococci, meningococci, gonococci, and staphylococci infections.

DOSAGE AND ADMINISTRATION: Suggested adult dosage is: initial dose 4.0 gm., followed by 1.0 gm. every four hours. Children: 0.2 gm. per kilogram of body weight (one-third of this amount initially, the remainder in five equal doses).

HOW SUPPLIED: Bottles of 100 and 1,000 tablets, 0.5 gm. each.

PRODUCER: Sharp & Dohme, Inc., Philadelphia 1, Pa.

WESTSAL

PURPOSE: Salt substitute.

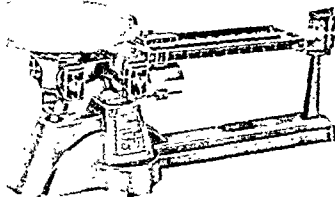
COMPOSITION: Contains lithium chloride, citric acid, and potassium iodide, and tastes exactly like salt.

INDICATIONS FOR USE: When sodium intake must be limited in congestive heart disease (and certain other heart conditions), certain renal conditions, hypertension, toxemias of pregnancy, cirrhosis of the liver, epilepsy, and in the Gerson diet in tuberculosis.

DOSAGE AND ADMINISTRATION: Sprinkled on the food at the table, or used in cooking and baking, according to the flavor desired by the individual.

HOW SUPPLIED: Special sprinkling bottles of 2 1/4 ounces.

PRODUCER: Westwood Pharmacal Corp., Buffalo 13, N. Y.



EDRYL

PURPOSE: For treatment of nasal congestion and sinusitis caused by gram-positive bacteria.

COMPOSITION: A concentrated solution of tyrothricin and ephedrine, with propylene glycol.

DESCRIPTION: The concentrate remains stable. Diluted 1:3 for use, Edryl supplies tyrothricin 0.02 per cent and ephedrine 0.5 per cent, and exerts powerful antibacterial effect despite presence of pus and mucus. Solution should be made fresh every two days to assure potency.

INDICATIONS FOR USE: To combat secondary gram-positive infections of the nose and sinuses following episodes of the common cold or allergic rhinitis.

CAUTIONS: Edryl (like other ephedrine-containing preparations) should be used with caution in coronary disease, hypertension, thyroid disease, or diabetes.

DOSAGE AND ADMINISTRATION: Administered with the Jetomizer (nasal applicator), the normal dose is two jets in each nostril. (Each jet delivers 2 to 3 drops.) For acute nasal congestion or ethmoiditis, two additional doses at five-minute intervals, repeating the dose every hour until congestion subsides. Dilute solution may also be given by atomizer or dropper.

HOW SUPPLIED: Bottles of 1 oz., with or without Jetomizer.

PRODUCER: Wyeth Incorporated, Philadelphia 3, Pa.

RUTAMINAL SCHENLEY

PURPOSE: Adjunctive therapy in arteriosclerosis, angina pectoris, coronary disease, and congestive heart failure.

COMPOSITION: Each tablet of Rutaminal contains aminophylline 1 1/2 gr.; rutin 20 mg.; phenobarbital 1/4 gr.

INDICATIONS FOR USE: For conditions manifested in structural and functional changes such as vascular spasticity, sclerosis, myocardial insufficiency and, of more recent interest, increased capillary fragility.

DOSAGE AND ADMINISTRATION: Recommended dosage is one or two tablets three or four times daily, preferably after meals. Duration of therapy depends on requirements of the patient. If required, the dose of rutin may be increased by supplemental use of Rutin Tablets Schenley, 20 or 60 mg. each.

CAUTIONS: Rutaminal is contraindicated for patients with severe impairment of renal or hepatic function and in Parkinson's disease.

HOW SUPPLIED: In bottles of 100 tablets.

PRODUCER: Schenley Laboratories, Inc., New York 1, N. Y.

OHAUS BALANCE

DESCRIPTION: The Ohaus Scale Corporation announces the availability of its new Triple Beam Balance featuring a stainless steel platform and beams. The Ohaus Triple Beam Balance is equipped with a stainless steel plate at the point of continuous usage—where all-element resistance is needed.

The beam calibrations are as follows: Front beam 10 by 1/10 gm.; center beam 500 by 100 gm.; back beam 100 by 10 gm. Sensitivity: Rated 1/10 gm.; actual 1/20 gm. Scale capacity: Scale capacity without attachment weights 610 gm.; scale capacity with attachment weights 2610 gm. Also available in an airdupois standard with decimal and fractional ounce calibrations.

PRODUCER: Ohaus Scale Corp., 10-14 Hobson St., Newark 8, N. J.

TESTOSTERONE PROPIONATE

PURPOSE: A steroid compound having definite androgenic characteristics, and usually considered to be the fundamental male sex hormone. Testosterone Propionate in Oil is a sterile solution for intramuscular use.

INDICATIONS FOR USE: Provides replacement therapy in conditions where there is a deficiency of androgens; in some cases, to counteract the stimulating effect of excess estrogens. Useful in hypogonadism, and female disorders.

HOW SUPPLIED: In 10 cc. Steri-Vials in two strengths: 25 mg. per cc., and 50 mg. per cc.

PRODUCER: Parke, Davis & Company, Detroit 32, Mich.

NEO-HOMBREOL

(M) Sublingual Tablets

PURPOSE: Sublingual tablets for buccal administration of male sex hormone therapy.

COMPOSITION: Each tablet contains 5 mg. of pure methyl testosterone.

DESCRIPTION: Neo-Hombreol tablets are absorbed through the mucous membrane of the mouth and provide androgenic effect when placed beneath the tongue or between the gum and cheek and retained until completely absorbed.

HOW SUPPLIED: Boxes of 30 and 100.

PRODUCER: Roche-Organon, Inc., Nutley, N. J.

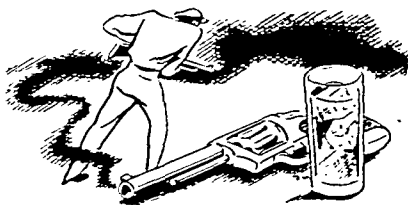
Leaves from a Doctor's Diary

By MAURICE CHIDECKEL

October 1 . . . He was no shining jewel in the diadem of his heritage. No doubts or fears beset him. He exemplified man's retreat from humanity, and he gave the lie to the theory that environment makes the child and shapes the man. He lied, stole and robbed, and possibly even killed. Like all gangsters—the products of our age—the exorbitant estimation of himself knew no bounds. As he lay dying from bilateral pulmonary hemorrhage following a gunshot wound, fully conscious, he told the stories of his escapades with sadistic zest. The administration of whole blood, donated by his brothers in crime, acted adversely as to the extent of the hemorrhage. He may have been given too much, which increased his blood pressure. His estranged wife now stood near him. He began to grow weaker. "Swear," he addressed himself to his wife, "that as soon as I am gone you will marry John the Bat." She shook her head negatively. "You once told me," she protested, "that he is a dirty rat, and that you hate him like poison." "That's why I want you to marry. . . ." The sentence was never finished. His comrades will see to it that she carries out his orders.

I watched those comrades, twenty of them, marching out of the hospital and it was a somnambulistic procession. Clumsy, slow-moving figures, their faces expressionless and lifeless, subhuman creatures that have no conception of the value of life, that of others or their own, creatures that repel. Viewing them, no one would ever suspect that these animalized beings con-

stitute a menace to society, and that at times they are complex and resourceful. One of the twenty killed the gangster who just died. Each knew who committed the murder. The secret will die with each. And I was thinking. The man in bondage to the bottle, the alcoholic, is proclaimed a sick man. Isn't the one in bondage to crime equally sick, or sicker? And is extermination the only prescription?



The nurse awoke me from my reverie. "Mrs. Pimschenholtz feels very bad." I rushed into her room. There stood her husband listening to her with unabated attention. "I will soon die," she spoke feebly. "Promise me that when you go to my funeral, you will ride in the same car with my mother." He scratched his head vigorously. "Well," he said and distorted his face, "if you insist. O.K. But I tell you I sure won't enjoy the ride." She disappointed him painfully. She did not die.

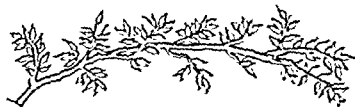
October 2 . . . At the age of 59, bachelor maiden Helen's life became suddenly crowded with romance and achievement. Her case was that of senile vaginitis with

bleeding—bleeding profusely at times. "What causes it?" she asked. I began: "In married women, intercourse may be a cause." She interrupted: "Can't intercourse be a cause in unmarried women too?" And soon her speech was entertaining and revealing. It proved to be a compound of wit, allegory and a sprinkle of real philosophy. "A body does not hurt anybody by having a little pleasure in life. What are we living for anyhow? Can't a girl use her private property as she likes? She sure can. Oh no, not him." She meant the dignified, prosperous-looking man in the waiting room, who came with her. "No. Can't with him. I am going to marry him. I've got to be innocent. Just got to. What? How did I get him? Well, it's quite romantic. It was in a crowded streetcar when he stepped on my foot. It hurt so badly I called him a rat. He said I was a hellcat. One word led to another, and when we left the streetcar we were engaged."

The comedy of human existence. Amusing and deceiving, banal and dull. Life, a brilliant landscape with many a radiance that sheds an unflickering light; with others only dark shadows, in which men seek an escape and never find it. It's lasting and unchanging, as Nature itself, and you can't do a damn thing about it.

* * *

October 5 . . . Ah, here is another maiden, not so pretty, Anita Fike, the aunt of a patient I was vitally interested in. Because of people like her, I long ago lost ardent faith in promises, and have found that realization is much preferable to anticipation. Hence I advised surgeon B.M. to collect his fee in advance. The operation was for patent ductus arteriosus of the adult type in a boy of 14. The surgeon's excision of the stenotic aorta and his end-to-end anastomosis of the two ends of the aorta were surgical masterpieces. Three weeks after the operation, the patient died from hemorrhage.



What the General Practitioner Should Know About Ophthalmoscopic Examinations

FREDERICK A. DAVIS*

UNIVERSITY OF WISCONSIN MEDICAL SCHOOL, MADISON

I HAVE long been interested in the teaching of ophthalmoscopy to undergraduate medical students. From the beginning of our teaching of the clinical branches at the University of Wisconsin Medical School, instruction in the use of the ophthalmoscope has been part of the course in physical diagnosis, at first a limited part but gradually becoming more extensive in subsequent years. The aims and purposes of our course are to instruct the student in the mechanics of the use of the ophthalmoscope and to acquaint him with certain fundamentals in diagnosis which might encourage him to continue the use of the instrument in his routine clinical work. The scope of this course is limited in the main to a study of the normal fundus, with later emphasis upon the more practical aspects of ophthalmoscopy which are important for the general physician.

Unfortunately, the time allotted for instruction in ophthalmoscopy in most of our medical schools is so short that it is virtually impossible to give the student more than a brief introduction to the subject. It is my belief that little progress can be made toward a more general use of the ophthalmoscope by the general practitioner until the student receives more instruc-

tion in its use during his regular undergraduate medical course. It is easy to outline the many fundus changes which are important for the general physician, but unless he has acquired considerable knowledge concerning the normal fundus and its variations and makes frequent use of the ophthalmoscope in his routine work, it is unlikely that he will develop sufficient confidence in his interpretation of the things he sees to obtain much benefit from fundus examinations. When studying the fundus, that wise saying, "We see only that which we know," is especially applicable, for we can look long and see little if we do not know how to interpret the things we see.

In my opinion the general practitioner should use the ophthalmoscope in his daily work, if we can but teach him how to use it. He should regard it as a useful adjunct to a complete study of a case, just as he would a blood count, or the use of an otoscope for inspection of the tympanic membrane, though it must be admitted that the technic of ophthalmoscopy is more difficult to acquire. Far too many general practitioners utterly disregard the ophthalmoscope and thereby overlook valuable information which is readily available to them in the study of their cases. This was particularly true of those physicians of a generation or more ago.

*Department of Ophthalmology, University of Wisconsin Medical School.

Some internists and most neurologists have long recognized the importance of the ophthalmoscope in the routine study of their cases. Many have acquired skill in its use and proficiency in the interpretation of fundus changes equal or superior to that of many ophthalmologists.

With the perfection of the modern electric ophthalmoscope the long and tedious practice which formerly was necessary to visualize the fundus has been largely eliminated. Skill in the use of the instrument can be acquired by anyone if he is willing to make the effort. I would like to emphasize from the outset, however, that there is no easy, quick road to mastery of ophthalmoscopic diagnosis. A thorough understanding of the structure of the tissues which make up the fundus oculi, some knowledge of the underlying disease processes which manifest themselves in these parts, and painstaking daily use of the instrument are essential for those who would derive satisfaction from ophthalmoscopic examinations.

It is obvious that there should be limitations in the use of the ophthalmoscope for general practitioners, since many pathologic changes encountered in the eye fall exclusively within the sphere of the ophthalmologist. I refer to various diseases involving the media of the eye, such as cataract and uveitis, and many diseases of the fundus which are largely ophthalmic problems. Many other diseases, however, are but local manifestations in the eye of common general diseases which are frequently seen by the general practitioner. Before entering upon a description of the technic of ophthalmoscopy let us first consider some of the basic rules which should govern everyone who uses the ophthalmoscope.

CONDITION OF MEDIA AND SIZE OF PUPIL

First, to obtain a satisfactory view of the fundus, the media must be clear. By that I refer to the cornea, aqueous, crystalline lens, and the vitreous. If there should be clouding of these structures from various causes, difficulty will be encountered in visualizing the fundus and consultation may be necessary.

Second, the size of the pupil is of great importance, especially when one is not skilled in the use of the ophthalmoscope. Should a clear view of the disk and retina prove impossible through the undilated pupil, a weak mydriatic such as euphthalmine, 3 per cent, or ephedrine, 5 per cent, may be used to relax the sphincter. A complete and thorough study of all parts of the fundus is usually impossible unless the pupil is dilated. These drugs produce a moderate dilatation of the normal pupil in fifteen to thirty minutes, although at times two instillations may be required if the iris is rigid. Their action is not excessive or prolonged and it can be quickly neutralized by the use of a drop of a miotic, such as pilocarpine, 2 per cent, or eserine, 0.5 per cent.

One should bear in mind that careless or indiscriminate dilatation of the pupil in subjects of 40 years or over may, in rare instances, precipitate an acute rise in intraocular pressure, such as is seen in acute glaucoma, in an individual already the subject of the disease in its early or latent stage, which has been unrecognized. Therefore, it is always wise to use a counteracting miotic at the conclusion of the examination whenever the pupil has been dilated for diagnostic purposes.

TECHNIC OF EXAMINATION

A few practical points concerning the technic of ophthalmoscopic examinations may be of assistance to those inexperienced in the use of the instrument.

Two methods of examination are employed by ophthalmologists—namely, the indirect and the direct. The indirect method permits a much more extensive view of the fundus at one time, without changing the position of the examiner's head. However, the image is much smaller or less magnified, and it is inverted. I shall omit any description of indirect ophthalmoscopy, since, in my opinion, this procedure is too complex for the general practitioner. It is of value to ophthalmologists who become proficient in its use.

The direct method, utilizing the electric self-luminous ophthalmoscope, is the simplest and most easily mastered technic yet devised. The image is erect and greatly magnified, so that fine details are easily recognized. I think it helpful for both patient and examiner to be comfortably seated in a dark or semi-dark room. The examiner should sit on an easily movable stool on the patient's right side when examining the right eye, and on his left side when examining the left eye. The examination is easier if the examiner's and the patient's heads are on approximately the same level. The patient should be told to look straight ahead or slightly to the nasal side, directing the gaze of the eye not under examination at some object, such as a white disk of paper pasted upon the opposite wall of the room.

The ophthalmoscope should be held vertically in the examiner's right hand before his right eye when examining the patient's right eye, and in the left hand before the left eye when examining the patient's left eye. With the instrument held close to his own eye the examiner should approach the patient's eye, at the same time steadying the patient's head by placing his hand on the back of the head or neck. The light from the ophthalmoscope is directed into the patient's pupil a few inches from the eye until a fundus-glow is seen. The examiner then continues to approach the eye as closely as possible without touching it, whereby details of the eye ground will come into view. If the examiner has a moderately high refractive error, he should wear his glasses, but they mechanically interfere somewhat with the examination and may be discarded if desired.



Figure 1. Direct ophthalmoscopy (from Duke-Elder, *Text-book of Ophthalmology*; C. V. Mosby Co., 1940-41).

temporal artery and vein, followed by the superior and inferior nasal vessels. In this way, one is less likely to overlook important changes in these vessels. If the patient has a high refractive error, a clear image may be possible only through adjusting the proper lens in the revolving disk of the ophthalmoscope to bring the retina into focus. This may be difficult or impossible when a high degree of astigmatism is present, for the image may then be blurred or indistinct. The May ophthalmoscope, Mayo model, is a very satisfactory instrument and is simple to operate.

OUTLINE OF BASIC FUNDUS CONDITIONS

I suggest that the general practitioner familiarize himself with the appearance of the fundus in the following five basic conditions:

1. He should know the normal fundus and its common variations.
2. He should be able to recognize abnormal blurring, congestion, swelling, or choking of the papilla, which is commonly seen in optic neuritis (papillitis) and in choked disk (papilledema).
3. He should be able to recognize pallor of the optic disk and varying degrees of atrophy, conveniently designated grades I, II, III, and IV.

AFTER the retina and retinal vessels come into view, one should follow the larger vessels to the point where they converge, viz., the optic disk or papilla. The disk is carefully scrutinized, then the surrounding retina, above and below, in and out, should be observed. It will be found helpful to adopt a systematic routine of study of the retinal vessels, starting with the superior temporal artery and vein, then the inferior

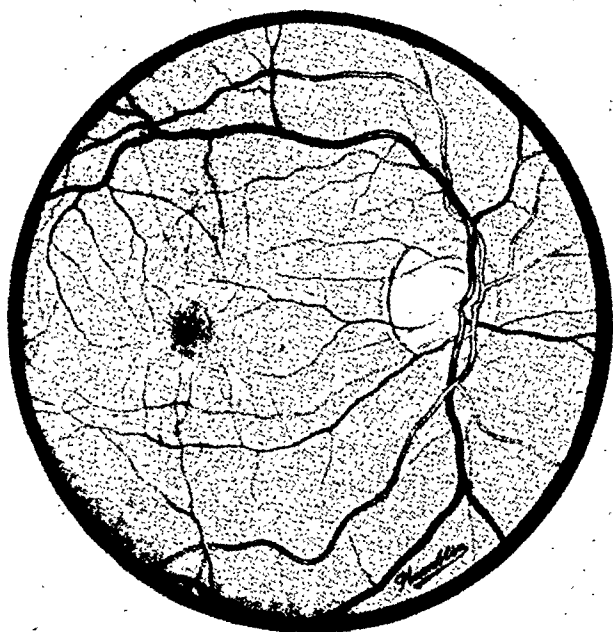


Figure 2. Normal fundus (from "The Anatomy of the Eye and Orbit" by Eugene Wolff, The Blakiston Co., Philadelphia).

4. He should be familiar with true glaucomatous cupping of the nerve head and be able to differentiate it from physiologic cupping.

5. He should be able to recognize abnormalities in the retinal vessels, particularly constriction or narrowing, spasm or obliteration, irregularities in caliber, tortuosity, beading, changes in color, arteriovenous compression, and hemorrhages and exudates in the retina.

Retinal hemorrhages and exudates frequently occur in the course of various general diseases, such as diabetes, hypertensive cardiovascular and renal diseases, the toxemia of pregnancy, etc. Their site, source, and character are varied, and the general practitioner may at first find it difficult to explore all their implications. It is important, however, for him to be able to recognize their presence; thereafter he may seek assistance concerning their nature and significance from someone more thoroughly trained in ophthalmoscopic interpretation.

THE NORMAL FUNDUS

There are many variations in the appearance

of the normal fundus as seen with the ophthalmoscope. Some knowledge of these variations is essential for the interpretation of the ophthalmoscopic image as seen in both the normal and pathologic fundus.

The fundus picture is naturally dependent upon the anatomic structure of the various parts which make up the background of the eye. Therefore it may prove helpful to review briefly the anatomy of this region and some phases of the embryologic development.

EMBRYOLOGY AND ANATOMY

As you will recall in your study of embryology, primary optic vesicles appear early in embryonic life as outpouchings from the lateral aspect of the forebrain, the cavity of the vesicles being directly continuous with that of the forebrain. Subsequent invagination of the vesicle occurs, producing the secondary optic vesicle, or optic cup. The outer layer of cells of the cup, which are made up of neural ectoderm identical with that which lines the forebrain, becomes enormously thickened from subsequent multiplication and differentiation of the cells, to form the major portion of the adult retina, while the inner wall remains thin and finally resolves itself into a single layer of pigmented cells to form the pigment epithelium of the retina.*

The layer of pigment epithelium has a very important influence upon the ophthalmoscopic appearance of the fundus. Since the retinal layers which lie anterior to it are transparent, the amount and character of the pigment in the cells largely determines the many variations which are encountered in the normal and in the pathologic fundus. More extended reference to this will be found in the description of the normal fundus. *Pari passu* with these changes, the stalk or pedicle through which the optic cup is attached to the forebrain becomes

*In later stages, when the eye is fully developed, the designation "inner and outer" layers is reversed, to correspond to their relative position with relation to the center of the eye, e.g., the pigment epithelium becomes the outer layer, and the remaining layers become the inner layers.

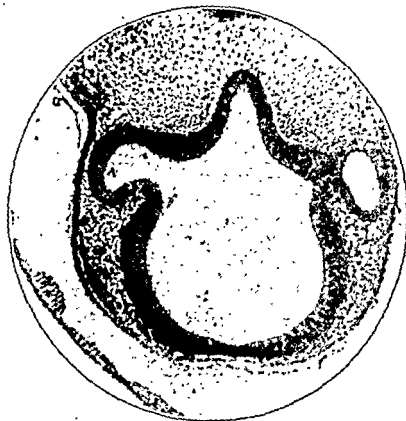


Figure 3. Forebrain and optic vesicles of embryo rabbit (from Von Hippel, E., in Axenfeld, Textbook of Diseases of the Eye; Gustav Fischer, Jena, 1923). Left shows wide open primitive stalk. Right shows partial closure of the stalk.

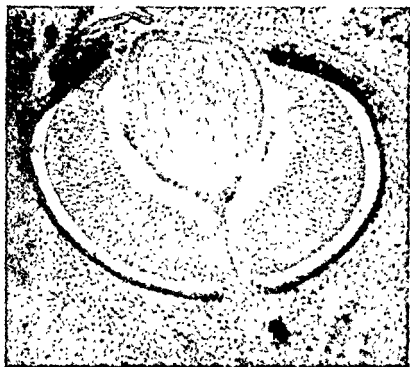


Figure 4. Embryonic eye of the shrewmouse (preparation of Professor Kolmer of Vienna). Specimen shows a more advanced stage than Figure 3. The layer of pigment epithelium is well developed. Nerve fibers can be seen extending back through the primitive optic stalk; also remnants of the hyaloid artery. Thick inner layer has shrunk away from outer pigment in preparation. Original cavity of optic vessel remains as a potential space and, therefore, throughout life becomes more easily separated in retinal detachment.

constricted, with final obliteration of the cavity of the vesicle and gradual elongation of the stalk to form the framework of the optic nerve. With subsequent growth of the surrounding mesoderm the outer coats of the eye ball (sclera

and choroid) are laid down, as well as the enveloping dura, arachnoid, and pial sheaths of the optic nerve and brain.* Nerve fibers originating in the ganglion cells of the retina extend back through the substance of the developing optic stalk to the midbrain, thereby forming this part of the optic nerve. Fibrous septa later extend into the nerve separating the nerve fibers into bundles.

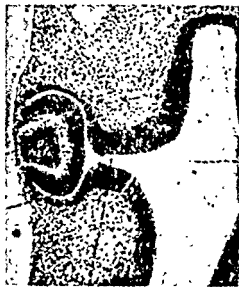


Figure 5. Optic cup of the rabbit (from Axenfeld, after Von Hippel, Textbook of Diseases of the Eye; Gustav Fischer, Jena, 1923). Note the cup is continuous with the cavity of the forebrain, the primitive optic stalk being open.

It is thus seen that the retina is but an expanded portion of the brain itself, and the optic nerve a fiber tract similar to those of the central nervous system. The nerve fibers of the tract arise from the ganglion cells of the retina and extend back to the brain. The anatomical structure of the individual nerve fibers differs

*The more complex changes incident to the formation and closure of the fetal ocular cleft or fissure are here omitted for brevity and simplicity of presentation.

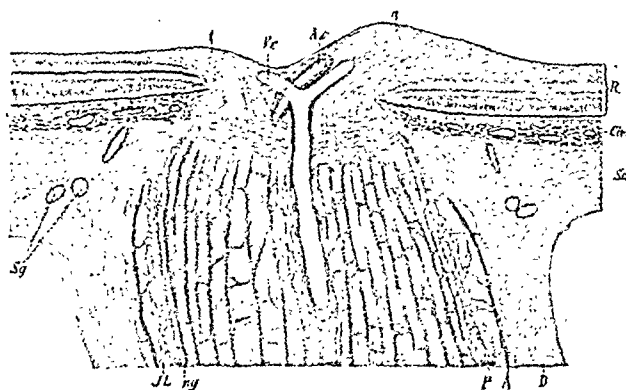


Figure 6. Longitudinal section through optic nerve, left eye (diagrammatic, from Axenfeld, after R. Graef, *Textbook of Diseases of the Eye*; Gustav Fisher, Jena, 1923). D: dura, A: arachnoid, P: pia, JL: intervaginal lymph-spaces, N: nerve fibers nasal to nerve fibers temporal side, Ac: central artery, Vc: central vein, Sg: scleral blood vessels.

from that of cerebrospinal nerves, being similar to that of the white matter of the brain. The sheaths of Schwann are absent, and the supportive framework is neurological.

The surrounding sheaths of the optic nerve—the dura, arachnoid, and pia—and their corresponding intervaginal spaces are continuous with those which envelop the brain. The dural sheath of the nerve passes over into the scleral coat of the eyeball, blending with its outer fibers. The thinner arachnoid likewise joins with and ends in the sclera. The pial coat hugs the nerve more closely and, in addition, sends prolongations into the body of the nerve, thereby contributing to the formation of the fibrous septa which separate the nerve fiber bundles. It also enters into the formation of the lamina cribrosa or the perforated opening in the sclera and choroid, through which the nerve fibers pass in their passage to and from the retina. These sheaths, together with their accompanying subvaginal spaces, form what might be called an optic nerve canal which ends blindly at the level of the lamina cribrosa and sclera.

The subdural and subarachnoid spaces are capable of distention, especially the latter, both experimentally and clinically. Changes in intracranial pressure are readily transmitted down the subvaginal spaces to produce swelling or

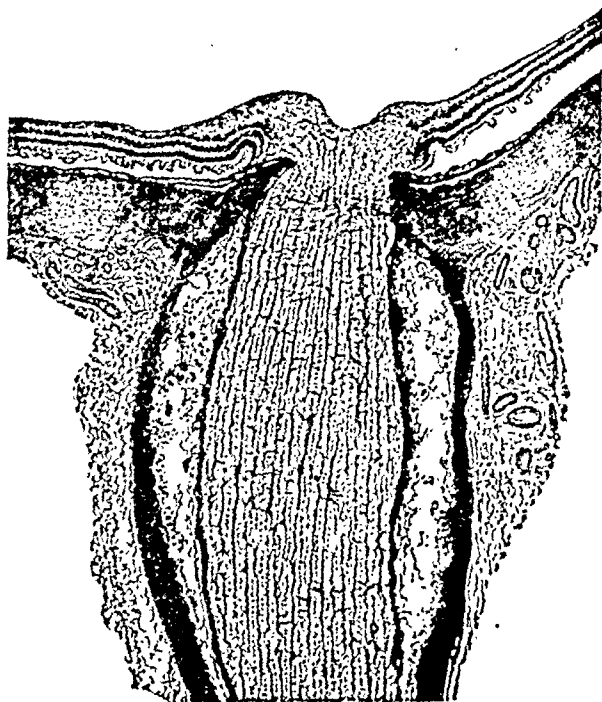


Figure 7. Choked disk from brain tumor (from Roemer, P., *Textbook of Ophthalmology*; translation of M. L. Foster; Reiman Company, 1917). Note swelling of the disk and distention of the intervaginal spaces of the sheath of the nerve.

choking of the optic disk, so commonly seen in various types of brain lesions. The lamina cribrosa is recognized microscopically by numerous fibers of connective tissue which appear to cut in transversely across the axis of the nerve. These fibers, as stated above, consist of connective tissue from the sclera as well as the inward prolongations of the pia.

THE PAPILLA OR OPTIC DISK

The optic nerve is divided into a nonmedullated and a medullated section. The medullated fibers end approximately at the lamina cribrosa which bridges the opening in the foramen opticum sclera et choroid. The nonmedullated section of the nerve is that portion lying internal to the lamina cribrosa. It is sometimes further divided into a retinal, choroidal, and scleral portion; these areas correspond to the coats of the wall of the globe through which



Figure 8. Microscopic section of optic nerve and papilla (Weigert stain) (from Guist, G.). Note dark staining of myelinated fibers of the nerve up to the lamina cribrosa, and decrease in size of the nerve internal to the lamina.

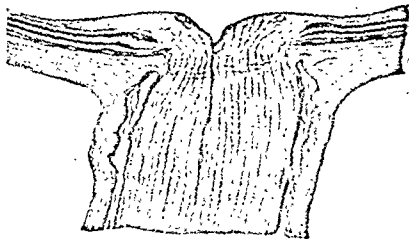


Figure 10. Small funnel-shaped excavation or cupping of the disk (diagrammatic) (from Adam, C., *Ophthalmoscopic Diagnosis*; translation of M. L. Foster, Reblman Co., 1913).

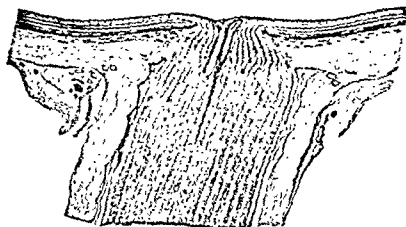


Figure 9. Microscopic section through normal optic nerve (diagrammatic) (from Adam, C., *Ophthalmoscopic Diagnosis*; translation of M. L. Foster, Reblman Co., 1913). The ophthalmoscopic appearance of this disk would appear uniformly pink or red with no cupping.

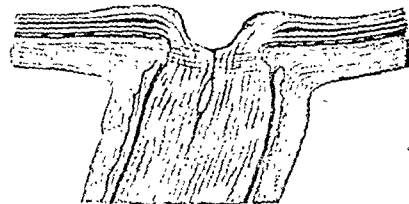


Figure 11. Deep physiologic cup (diagrammatic section) (from Adam, C., *Ophthalmoscopic Diagnosis*; translation of M. L. Foster, Reblman Co., 1913).

the optic nerve passes. I describe this region in some detail, since that part of the nerve which lies anterior to the lamina cribrosa makes up what we see with the ophthalmoscope and what we designate the disk, optic nerve head, or papilla. The lamina cribrosa is frequently visible at the bottom of the disk.

The foramen or opening in the sclera and choroid is approximately 1.5 mm. in diameter and varies slightly in form and contour from round to oval. The disk or intraocular

portion of the nerve head which is visible with the ophthalmoscope is likewise round or oval and is made up of the nerve fibers which, beyond its borders, are spread out upon the inner surface of the retina. The surface of the disk varies. It may be smooth and flat, or it may show a funnel or a cup-shaped depression.

The flat papilla or disk is one in which the opening of the scleral canal is of such size that the nerve fibers completely fill up the foramen opticum sclerae and, therefore, little or no depression is present. This anatomical condition produces the reddish-pink disk seen with the ophthalmoscope, sometimes producing an appearance known as a pseudoneuritis.

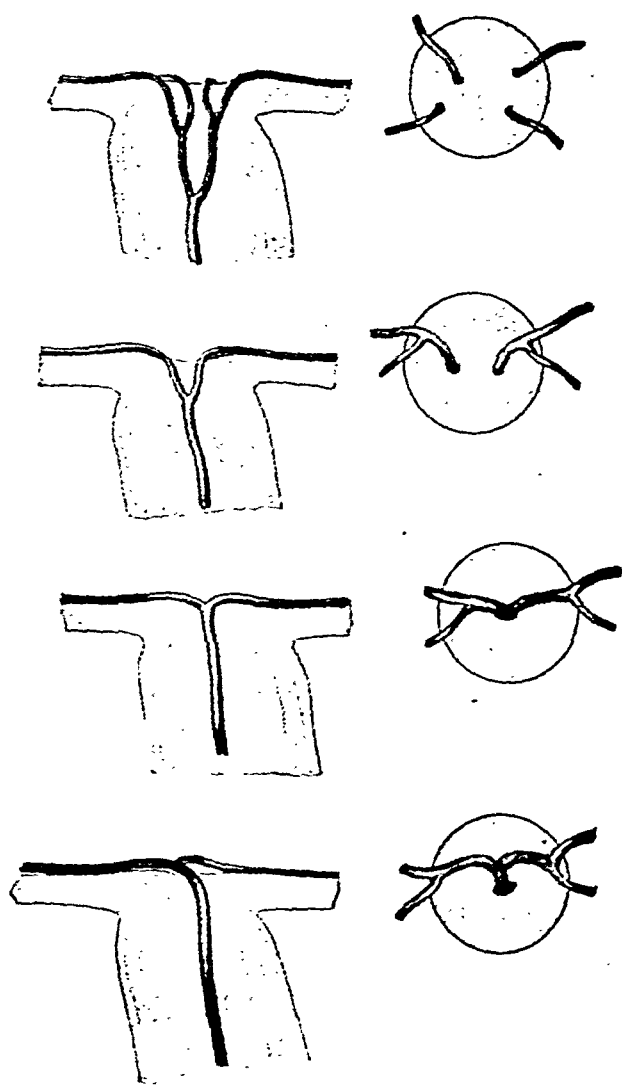


Figure 12. Schematic drawing of varied distribution of retinal vessels on the disk (from Adam, C., *Ophthalmoscopic Diagnosis*; translation of M. L. Foster, Rebman Co., 1913). When the vessel divides within the nerve the second and third divisions appear on the disk.

The excavated disk is one in which there is a funnel-shaped, cuplike depression in the center or, more frequently, slightly to the temporal side of the disk, commonly called the physiologic-cup. This funnel- or cup-shaped depression occurs because the optic nerve fibers do not completely fill up the foramen opticum sclerae or hole in the scleral wall. They cling to the

wall of the canal as they spread out upon the retina, and thus a central depression may remain. At times the cup is quite large and deep, though it does not reach the margin of the disk in the normal disk. The abrupt change in the size of the optic nerve as it enters the lamina cribrosa also contributes to the cupping, since the nerve becomes much smaller at this point owing to loss of the medullary sheathing of the individual nerve fibers; thus the bulk of the tissue which fills the scleral opening is reduced. The lamina cribrosa is thus visible at times at the bottom of the cup, as seen with the ophthalmoscope. Atrophy of the embryonic papilla of Bergmeister may also contribute to the formation of the physiologic cup.

The central retinal artery and vein reach the retina through the center of the nerve and are seen at the side of bottom of the cup if it is present; otherwise they appear to spring from the center of the nerve head or slightly to the nasal side. The main branches may divide within the nerve, or in the cup, or on the surface of the disk.

Knowledge of the anatomic variations in the tissues about the margins of the disk is essential for a thorough understanding of the ophthalmoscopic appearance, which may vary considerably within normal limits. In most eyes the layers of the choroid and retina surrounding the disk end at the disk margins. The marginal outlines are thus usually sharply defined, but in some instances the choroid and retina may stop a little short of the actual margin of the disk and thus a white circle, ring, or crescent may be seen just outside the pink area of the disk itself. This is called a scleral ring or crescent, and it appears because the overlying choroid and retina are absent in this area; thereby the border tissue becomes visible.

At times a black pigmentation is seen about the disk as a complete circle but more frequently as a crescent. This is due to the arrangement of the pigment epithelium of the retina. It may be unusually thick at this point, or it may project slightly beyond the overlying retinal layers and beyond the choroid. Since the retina and nerve fibers are transparent, the

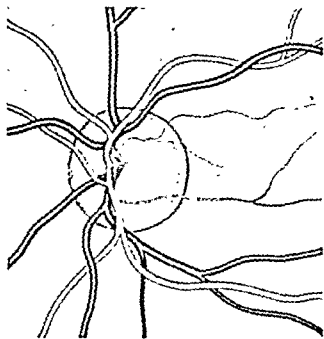


Figure 13. Scleral crescent with pigment ring (from Aveneteld, after Elchning, A. Textbook of Diseases of the Eye: Gustav Fischer, Jena, 1923).

pigment shines through these structures and consequently it appears black. At times, more extensive white or pigmented crescentic areas of a pathologic nature, known as *conus*, border the disk. This type of crescent is frequently seen in high myopia.

Sometimes the nasal side of the disk is blurred, while the temporal side shows a wide white crescent. This is due to elongation of the globe and a stretching or displacement of the retina whereby it is pulled over and conceals the disk nasally, while on the temporal side the border tissue and the sclera become exposed and appear white. This condition is commonly referred to as traction and distraction or supertraction crescents.

THE RETINA AND CHOROID

It is not intended to enter into any detailed description of the histologic structure of the retina and choroid, since it is not essential for the general practitioner. No doubt most of you in your student days memorized the names of those 10 complex retinal layers for final examination in anatomy. The study of the structure of this delicate, transparent, filmlike coat, approximately 0.5 mm. in thickness, which lines

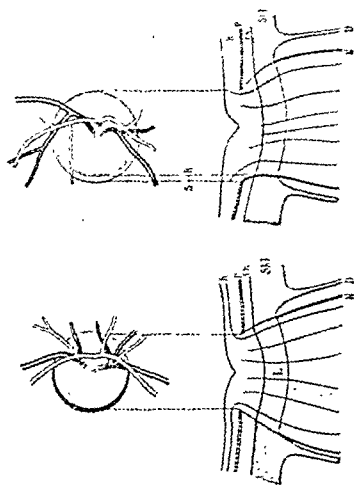


Figure 14. Diagrammatic drawing showing pigment crescent (bottom) and scleral crescent (top) (from Aveneteld, after Elchning, A. Textbook of Diseases of the Eye: Gustav Fischer, Jena, 1923).

the inner surface of the posterior part of the eyeball is a fascinating field for the ophthalmic histopathologist. However, anyone who undertakes ophthalmoscopic examinations will obtain greater satisfaction from them if he has some knowledge of the retinal architecture; without this knowledge he will have little appreciation of what he sees.

AS PREVIOUSLY described in the development of the eye, the retina may be divided into two main divisions: (1) the layer of pigment epithelium, and (2) the remaining nine layers which lie anterior to it (Figures 5 and 18). Since the inner layers are transparent in the normal state, they are virtually invisible when viewed with the ophthalmoscope, except for the retinal vessels which traverse them. Therefore, it is the layer of pigment epithelium, made up of a single row of hexagonal pigmented

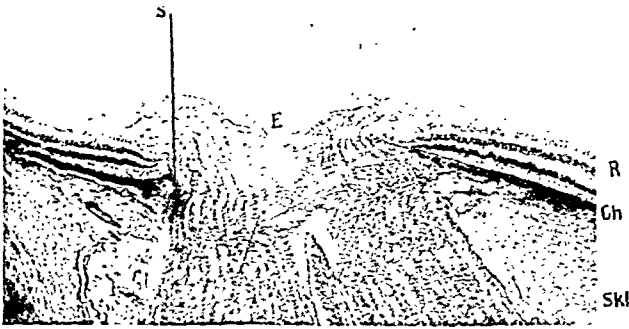


Figure 15. Microscopic section of normal nerve head (from Guist, G.). Showing histologic basis for pigmented crescent or ring bordering disk. R: retina, Ch: choroid, Sk: sclera, E: physiologic excavation, S: layer of pigment epithelium projecting inward beyond other retinal layers.

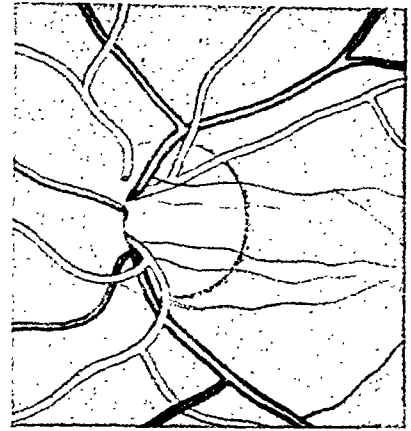


Figure 16. Temporal conus in myopia (from Axenfeld, after Elschning, A., *Textbook of Diseases of the Eye*; Gustav Fischer, Jena, 1923). Traction and distraction crescents due to stretching incident to the myopia.

cells, which largely determines the variations encountered in the normal fundus. If the melanin pigment which is present in these cells is heavy and densely packed, nothing can be seen of the adjacent choroid which lies beneath it. However, if the pigment is lightly distributed or is absent, as in the case of albinism, the choroid, and at times the sclera, may become visible.

The choroid is a thin, soft, brown coat which measures approximately 0.25 mm. in its thickest area. It is extremely vascular, being largely made up of vessels and pigmented cells. The chief function of the choroid is to provide the right blood supply to the outer layers of the retina, viz., the rods and cones. The blood vessels of the choroid and the intervening masses of dense pigment are frequently visible with the ophthalmoscope when the pigment epithelium of the retina is thin or absent.

OPHTHALMOSCOPIC APPEARANCE OF THE NORMAL FUNDUS

The appearance of the normal fundus may vary considerably in different individuals, depending upon age, complexion, race, etc. It is, therefore, important that you become familiar with these variations in order that you may not confuse them with pathological changes.

Systematic writers frequently describe the

normal fundus under three different types, to which I should like to add a fourth: (1) the uniform stippled fundus, (2) the tassellated fundus, (3) the albinotic fundus, and (4) the mixed-type fundus.

These variations depend, in a large degree, upon the amount, type, and distribution of the pigment in the choroid and the pigment epithelium of the retina. The intensity of the pigmentation usually follows the color of the hair and skin of the individual, varying with the blond and brunette types.

1. The uniform stippled fundus has a uniform red color, varying somewhat with the amount of pigment present. The color may be a deep, brownish-red, or slate gray in the dark-skinned races, e.g., the negro, or it may be a yellowish-red in the yellow races. The pigmentation is usually more dense surrounding the disk and in the macular region.

In younger subjects, especially hyperopes, fleeting shotlike reflexes from the surface of the retina may flit across the surface of the retina as the light is moved about over it. The light is so reflected because of inequalities in the surface of the retina owing to the underlying vessels. The stippled type of fundus is produced by the dense and uniform pigmen-

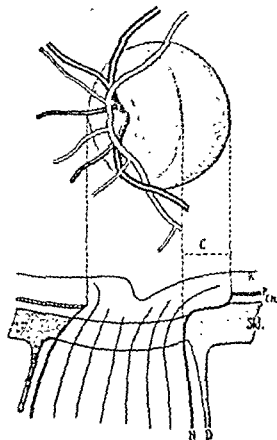


Figure 17. Temporal conus (from Asensfeld, after Elschnig. A. Lehrbuch und Atlas der Augenheilkunde; Gustav Fischer, Jena, 1923). C: conus, R: retina, P: pigment epithelium, Ch: choroid. Skl: sclera.

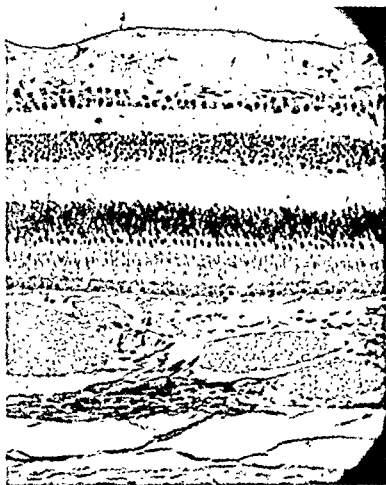


Figure 18. Section through the normal human retina and choroid. Preparation of Dr. E. E. MacEwen (from a photograph supplied by Dr. James Shields). Layers of retina: 1. Pigment epithelium; 2. Rods and cones; 3. External limiting membrane; 4. Outer nuclear layer; 5. Outer molecular layer; 6. Inner nuclear layer; 7. Inner molecular layer; 8. Ganglion cells; 9. Nerve fiber layer; 10. Internal limiting membrane.

tion of the pigment epithelium, which conceals the underlying choroid.

2. The fassellated or tigroid fundus is frequently encountered and appears as a dark brown or gray mottling on a bright red-streaked background. It occurs when the pigment epithelium of the retina is but lightly pigmented. The masses of choroidal pigment appear as dark, irregular islands on a bright red background. The bright red areas are made up of choroidal vessels which interlace, anastomosing freely and running in every direction. Extreme types of the tigroid fundus might easily be mistaken for choroiditis by those who are unfamiliar with it.

3. The albinotic fundus is characterized by the complete absence of pigmentation in both the retina and the choroid, so the varied pattern of the choroidal vessels becomes visible against the white or yellowish background of the sclera.

The choroidal vessels are distinguished from the retinal vessels by their uniform, bright pink color, by the absence of a light reflex in the vessels, and by their abundant anastomoses. The vessels lie deeper than the retinal vessels, and they have a flat, bandlike contour. At times albinism may be incomplete or partial, with only certain areas of the retina involved. Although the albinotic fundus is usually classified as a normal type, high myopia often accompanies it, and frequently the visual acuity is markedly impaired.

4. The mixed-type fundus is very frequently encountered. In this type the uniform stippled condition prevails over the larger part of the central area and surrounds the disk, but toward

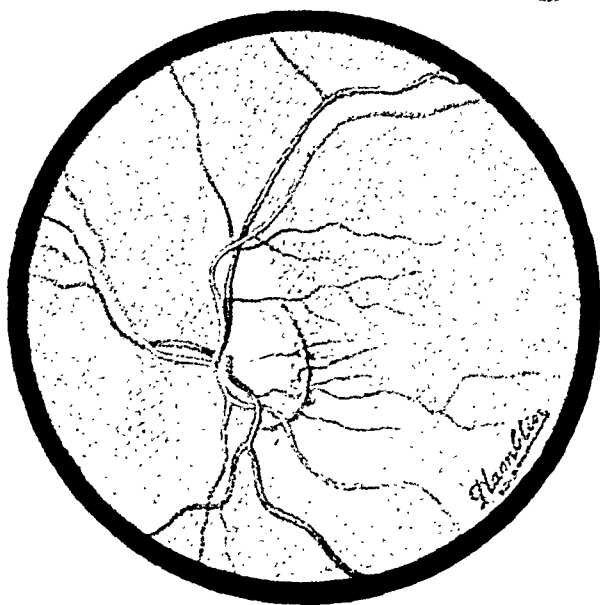


Figure 19. Opaque (medullated) nerve fibers (from Mann, Ida, *Developmental Abnormalities of the Eye*; Cambridge University Press, England.) Used by permission of The Macmillan Company, New York.

the periphery of the fundus the choroidal vessels are frequently visible owing to a thinning of the pigment in this area. This condition is present in quite a high percentage of the fundi of normal individuals seen in routine fundoscopic examinations following refraction.

THE macula is located in the line of the visual axis at the posterior pole of the eye. Its center, the fovea, lies about 3.5 mm. or $2\frac{1}{2}$ disk diameters to the temporal side of the disk and slightly below the horizontal meridian. It is the most sensitive part of the retina and its structure is so arranged as to permit maximum visual acuity only in this area. It is devoid of retinal blood vessels, being nourished by the underlying choriocapillaris of the choroid. The macula is often shown in textbooks as an oval area somewhat larger than the disk itself. Anatomically this is correct, but ophthalmoscopically the entire macular area is rarely visible. Occasionally in young subjects a bright oval reflex, like a halo, is seen at the periphery of the macular



Figure 20. Medullated nerve fibers (Weigert Pal stain) (from Axenfeld, after Elschnig, A., *Textbook of Diseases of the Eye*; Gustav Fischer, Jena, 1923). Note medullated fibers stained dark.

area, but full details of this region are visible only with special illumination, such as red-free light. With this method, the yellowish coloration from which it derives its name, macula lutea, can be seen.

The usual ophthalmoscopic appearance of the macula consists of a small white spot surrounded by an area more deeply pigmented than the rest of the retina. This white spot is nothing but a reflex from the curved surface of the macula at the fovea. Its form and shape change, therefore, as the light from the ophthalmoscope is moved in different positions. The sharp contour and brightness of the reflex usually diminishes with advancing years. The macular area can be best observed if the patient is directed to look at the light in the ophthalmoscope, providing the pupil is well dilated. If the pupil is not dilated, this procedure is not satisfactory, since the pupil will contract sharply, and the light reflex from the cornea may prove annoying or may make it impossible to view the macula under these conditions. The inexperienced may have to search for the macula and may find it helpful to note that the fine terminal retinal blood vessels which surround this area point toward it but end before reaching it.

THE DISK OR PAPILLA

The optic disk or papilla is the point of greatest interest in the fundus. It may be located by

following the larger vessels to the point where they converge or emerge on the surface of the retina. It can best be observed if the patient is directed to look slightly in, or nasalward, since it lies to the nasal side of the visual axis and is, therefore, out of line when the examiner looks into an eye whose gaze is directly forward.

WHEN examining the disk it is well to keep in mind the following points: (1) form and size, (2) color, (3) margins, (4) surface level (excavation or protrusion), and (5) blood vessels.

1. The disk is usually round or slightly oval. There is, at times, an apparent variation in size, the disk being smaller in high degrees of hyperopia (farsightedness) and larger in high degrees of myopia (nearsightedness). Its shape may be distorted in high degrees of astigmatism when it is frequently elongated and somewhat blurred or indistinct, occasionally so much so as to be classified as a pseudoneuritis.

2. The color of the disk is variable. It is usually light pink in color and somewhat paler than the surrounding retina. This varies, however, depending upon its contrast with the color of the surrounding retina. It has a paler pink hue in the dark stippled fundus of the brunette, and a reddish-pink color in the pale fundus of the blond. The temporal half of the disk is somewhat paler than the nasal, in part due to the presence of a physiologic cup. Since the nerve fibers are spread apart in the cup, a part of the lamina cribrosa becomes visible at the bottom of the cup. The nerve fibers in the temporal half of the disk are finer and fewer in number, since they are limited to a group of fibers which make up the papillomacular bundle which supplies the macula. The nasal half of the disk has a deeper pink color owing to the presence of a greater number of nerve fibers in this area; consequently, the greater number of fine blood vessels or capillaries, which accompany the nerve fibers, impart a deeper pink hue to it.

3. The disk margins are usually fairly sharp-

ly defined, but the superior, inferior, and nasal borders are less distinct than the temporal due to the greater number of nerve fibers which pass over these areas. The arrangement of the nerve fibers of the temporal half of the retina is such that most of them by-pass the macular area and thus reach the disk above and below by a peculiar arcuate bending which crowds the fibers at the superior and inferior borders of the disk. At times the blurring produced by this is so marked as to raise the question of a neuritis, which must be ruled out by further study of the visual acuity and fields. When the physiologic cup is entirely absent the disk may appear congested, with a blurring of all the disk margins, thus producing yet another condition known as pseudoneuritis.

Medullated nerve fibers rarely extend beyond the lamina cribrosa and are seen ophthalmoscopically as intensely white patches adjoining the disk. They have a characteristic, silky, white, striated appearance, the outer edges resembling the fine hairs of a paint brush. They lie in the nerve fiber layer of the retina and frequently cover the adjacent retinal vessels. They remain stationary throughout life and produce no loss of visual function aside from an enlargement of the blind spot in the area involved.

4. The surface of the disk is usually level with that of the surrounding retina excepting only the area of the physiologic cup, which is depressed. The cup may appear as a slightly cone-shaped depression or it may take the shape of a sharp, deep, punched-out cup. When the cup is large and deep, the bundles of nerve fibers become visible at the bottom of the cup as gray spots in contrast to the intense whiteness of the lamina itself. This is due to the fact that the nerve fibers lose their myelin sheaths as they enter the lamina; they are more translucent and, therefore, reflect less light than the surrounding connective tissue.

If the physiologic cup is quite large, it may be confused with the pathologic cupping seen in glaucoma. The criterion for differentiation of the physiologic cup from that of glaucoma is that the former does not extend to the border

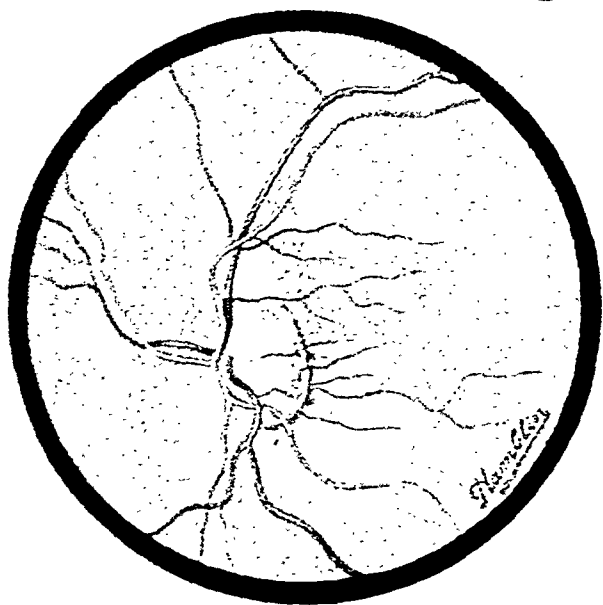


Figure 19. Opaque (medullated) nerve fibers (from Mann, Ida. *Developmental Abnormalities of the Eye*; Cambridge University Press, England.) Used by permission of The Macmillan Company, New York.

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THE DISK OR PAPILLA

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When the inflammatory process affects the nerve head or the papilla, it is commonly called papillitis; when it is confined to the trunk of the nerve, it is termed retrobulbar neuritis. Since retrobulbar neuritis rarely shows any ophthalmoscopic evidence of the acute inflammatory phase of the disease, I shall omit any extended discussion of it. A residual pallor of the disk, especially of the temporal half, which appears some time after the acute process has subsided, may be the only ophthalmoscopic change seen. Multiple sclerosis is responsible for the great majority of these cases and usually occurs in persons under thirty. It is typically unilateral and is sudden in onset; it causes a rapid loss of vision, and presents a normal-appearing nerve. I have recently seen a case, however, in a young woman, thirty years of age, who had a typical mild papillitis.

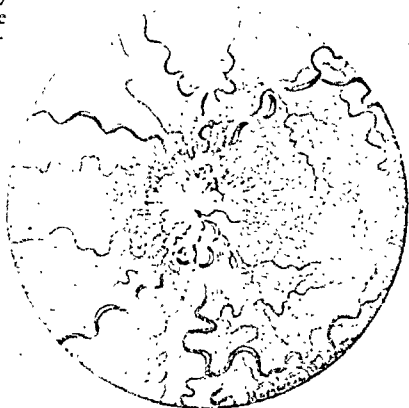


Figure 21. Papilledema (choked disk) (from de Schweinitz, G. E., *Diseases of the Eye*; W. B. Saunders Co., 1916). From a patient with tumor of the brain.

INTRAOCULAR neuritis or papillitis is a relatively common disease. The first ophthalmoscopic evidence of the disease is hyperemia of the disk. The margins become blurred and indistinct, and the veins slightly engorged. The hyperemia is rapidly followed by a mild degree of swelling, usually not over two to three diopters, though occasionally more. Flame-shaped hemorrhages appear on the disk and immediately around it, and at times edema and some exudates appear in the adjacent retina. The disease is usually preceded by marked reduction in central visual acuity. This may develop before there is any ophthalmoscopic evidence of the disease. The onset may be sudden or gradual. As a rule the disease is transient, and recovery may take place in a few weeks under proper treatment. In mild cases remarkable and complete restoration of vision may follow, with only slight residual pallor of the nerve. In others there is severe damage to the nerve fibers with marked optic atrophy and permanent loss of vision.

CHOKED DISK OR PAPILLEDEMA

The term choked disk or papilledema is used when swelling or protrusion of the nerve head

arises from increased intracranial pressure. It is primarily a passive edema of the disk, unassociated with any inflammatory change; for a considerable period there may be no disturbance of visual function. Papilledema, therefore, has a different etiology from optic neuritis or papillitis, and a different pathology and symptomatology, although the appearance of the two states may be indistinguishable ophthalmoscopically in certain stages of the two affections. This is especially so either in the early stages of choked disk or in mild cases. Careful evaluation of various other associated symptoms may be necessary to arrive at a correct diagnosis. Early reduction in visual acuity, which at times may be profound, is characteristic of papillitis, whereas in papilledema the visual acuity may be but slightly affected for a considerable period of time.

Intracranial pressure arising from brain tumor is responsible for papilledema in a great majority of cases. Not infrequently it is a relatively late symptom, however. It may also develop in connection with various other le-

ected before the other. The atrophy develops slowly, with a gradual loss of vision. Vision may be surprisingly good, however, at times when the nerve appears quite white, a circumstance not infrequently found in other forms of optic atrophy. According to the present most popular view the atrophy arises as a result of a peripheral and interstitial neuritis produced by the treponoma of syphilis and its toxins which cause secondary degeneration of nerve fibers.

Although the classical description of the ophthalmoscopic appearance of the disk is gray or gray-green, it not infrequently is white, and the appearance is indistinguishable from that of any other primary atrophy. The retinal vessels are little affected in the earlier stages; later they become narrowed. The remainder of the retina may appear essentially normal for a time. Eventually thinning may occur from atrophy of the ganglion cells.

The general physician should never fail to study the fundi of patients with small, rigid pupils which are inactive to light but contract in accommodation—a characteristic of the Argyll-Robertson pupil—since optic atrophy is so frequently encountered with this symptom. Many other fundus changes due to syphilis might be mentioned but are really beyond the scope of this paper.

The physician should be on the alert for temporal pallor of the disk, commonly seen after repeated attacks of multiple sclerosis. He should also be familiar with the slight temporal pallor associated with the large physiologic cup, previously referred to, otherwise he may confuse this with pathologic changes. Ophthalmologists frequently describe the pallor of optic atrophy as grades I, II, and III, a somewhat rough but convenient method of indicating the degree of atrophy present.

CHRONIC SIMPLE GLAUCOMA

It may appear strange to some that I include the fundus picture of glaucoma among the "must" rules laid down as essential for the general practitioner. I insist that this is highly proper, for unless the ophthalmologist can en-

list the aid of the general practitioner in the early recognition of this disease, there seems little hope of reducing the incidence of blindness resulting from it. A program of publicity for the lay public might help, but here again the practitioner would be of great assistance, since many apprehensive individuals will seek advice from him once they are aware of the danger of the disease.

In my experience blindness from chronic simple glaucoma seems to be by no means lessening. Approximately 12 per cent of all blindness is attributed to glaucoma, and in the upper age groups (over 45 years) the percentage is probably much higher, though accurate statistics are difficult to obtain.

How can the general practitioner help in this program for preservation of vision? If he makes daily use of the ophthalmoscope, he may learn to recognize the early stages of cupping of the optic disk which accompanies the disease. Although it is admitted the disease may be relatively advanced when cupping has become evident with the ophthalmoscope, a considerable measure of vision can nevertheless be preserved even at this late date if atrophy is not advanced. It is unquestionably too much to expect the general practitioner to become familiar with other signs which appear in the early stages of the disease, such as increase in intraocular pressure, shallowness of the anterior chamber, and the various changes in the visual fields, but I feel he can, with some training and effort, learn to recognize the glaucoma cup.

As a rule, patients with acute glaucoma consult an oculist, since pain in and about the eye is so acute and agonizing that they seek relief. However, the pain is at times referred to the temples, face, teeth, and other parts of the head, and is frequently accompanied by vomiting. I have known cases which were under treatment by the general practitioner for stomach trouble for a considerable time before it was discovered that the eye was involved. He should be on the alert for this fulminating type. However, the

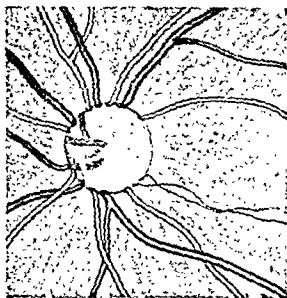


Figure 24. Glaucoma cup—total (from Axenfeld, after Elschnig, A., *Textbook of Diseases of the Eye*; Gustav Fischer, Jena, 1923). Note fundus is of the "tasseled type."

fundus usually cannot be visualized in acute glaucoma due to steaminess of the cornea, so the ophthalmoscopic examination may be unsatisfactory or impossible.

Chronic simple glaucoma, or glaucoma simplex, sometimes referred to as "compensated glaucoma," is frequently without symptoms of any kind for a considerable period in the course of the disease. This results chiefly from the fact that the rise in intraocular pressure is gradual thereby allowing the tissues of the globe to become adjusted to the pressure, and inflammatory symptoms do not develop. It is not at all uncommon for a patient to be brought to the office almost totally blind, except for a small telescopic field, unaware that he had the disease. To be sure he has been conscious of gradually failing vision (often mistaken for cataract), but frequently he has not been fully cognizant of this, since central acuity or the ability to read ordinary print may be preserved for a very long time, even though the disease is gradually progressing. This is due to the fact that the disease first affects the peripheral field, especially on the nasal side, with some other well-known peripapillary field defects, while the central vision is spared almost to the end. Optometrists who examine large numbers of

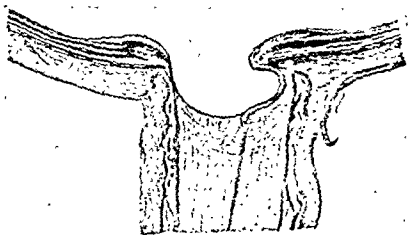


Figure 25. Deep glaucomatous excavation (from Adam, C., *Ophthalmoscopic Diagnosis*; Rebman Company, 1913). Note complete destruction of nerve head from intraocular pressure.

patients for glasses usually are totally ignorant of fundus pathology except for some of the more recent graduates who are showing some progress in this regard. The general physician should, therefore, make every effort possible to increase his knowledge of the disease.

THE GLAUCOMA CUP

The cupping of the disk in glaucoma is, as a rule, easily recognized although there are borderline cases in the early stages in which it is impossible to differentiate it from the physiologic cup, and many other tests are then required to establish the diagnosis. The typical cup is relatively large. At first it occupies the central and temporal portions of the disk, but eventually it expands to involve the entire disk. The margins of the cup are usually sharply defined, and the sides are steep, so that it presents a definite punched-out appearance. Blood vessels which enter the cup are often pushed to the nasal side. They hug the sides of the cup and dip down beneath its overhanging edges to disappear partly from view as they curve around it. They reappear in the bottom of the cup and can be brought sharply into focus by adjusting the lenses in the ophthalmoscope. When the disease is not far advanced and the cup is relatively shallow, it presents a uniform gray color; as the cup deepens, however, atrophy

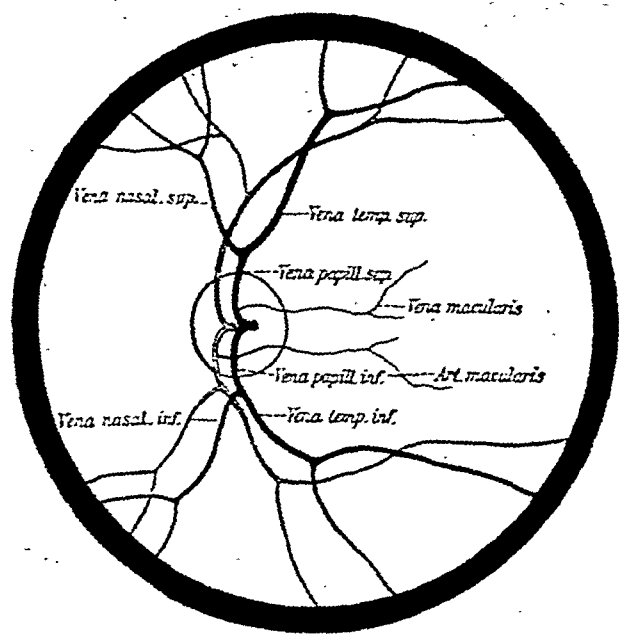


Figure 26. Schematic drawing of ophthalmoscopic appearance of retinal vessels (from Adam, C., *Ophthalmoscopic Diagnosis*; Reisman Company, 1913).

of the nerve fibers progresses, and the entire area becomes white.

When the increased intraocular pressure is of long standing, the pigment of the retina and choroid becomes thinner. This may be so marked immediately surrounding the disk that the sclera may be partly exposed. This condition is recognized ophthalmoscopically as a white circle bordering the disk, known as the glaucoma halo. This term should not be confused with the well-known colored halo observed by the patient when he looks at artificial lights at night. The latter occurs more frequently in the prodromal stage of acute glaucoma, but it also occurs at times in chronic simple glaucoma when the intraocular pressure rises sufficiently to induce edema of the cornea, which accounts for the phenomenon.

The retinal vessels may show only slight change. The arteries become somewhat narrower; the veins are frequently slightly engorged. Pulsation may appear in the central artery on the disk, though this is of little diag-

nostic significance since it occurs in a number of other conditions and, rarely, in healthy eyes.

RETINAL VASCULAR DISTURBANCES

THE remainder of this paper will be devoted to various common retinal changes that are of interest to the general practitioner. Some of these changes will be discussed at length, since they are of great importance not only in ophthalmoscopy but in the diagnosis of other diseases.

Retinal vascular changes furnish important clues in the early diagnosis and prognosis of many diseases of interest to the general practitioner, particularly the cardiovascular-renal diseases. The diagnosis of such affections as arteriosclerosis and essential hypertension may be greatly facilitated by careful and painstaking study of the retinal vessels.

Some physicians consider information gained from ophthalmoscopic studies in these diseases to be of greater value than any other single diagnostic procedure. Certainly no other means of examination affords the direct visual evidence of vascular changes that is offered by the ophthalmoscope.

When viewing the retinal vascular system it is well to remember the extremely small size of the vessels. The caliber of the retinal arteries is such that they should be classified as arterioles. The diameter of the central retinal artery is about 0.25 mm., or 1/100 of an inch, but due to the magnification of the dioptric system of the eye the apparent size of the vessels when viewed with the ophthalmoscope is increased to approximately 1 to 1.5 mm., varying according to the refractive error of the eye. The veins being slightly larger and much darker in color are more readily visualized. The light streak which traverses the vessels is a striking feature, especially in the larger branches. It is brighter and wider in the artery than in the vein. The veins follow the course of the arteries in a rough way, though the vessels may cross and recross each other in their course.

In healthy individuals the contour of the vessels is usually perfectly smooth and regular, showing no variation in caliber, except that

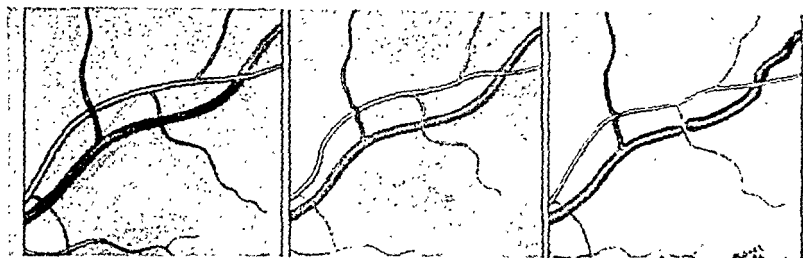


Figure 27a. Normal vessels. Caliber of artery: average. Caliber of vein: average. Reflex stripe on artery: moderate. Lumen of artery: regular. Compression of vein at arterial crossing: none.

Figure 27b. Senile fibrosis. Caliber of artery: constricted. Caliber of vein: normal or constricted. Reflex stripe on artery: normal or mildly exaggerated. Lumen of artery: regular. Compression of vein at arterial crossing: none or mild. Sclerosis or choroidal arteries often associated.

Figure 27c. Signs of hypertension. Caliber of artery: uniformly constricted. Caliber of vein: normal or relatively dilated. Reflex stripe on artery: uniformly exaggerated. Lumen of artery: regular. Compression of vein at arterial crossing: moderate.

they gradually become smaller as they extend farther from the disk to the periphery of the retina. Moderate tortuosity of both arteries and veins is commonly seen in healthy individuals. At points where the vessels cross each other there is no deviation in their course nor is there any change in their size and contour. In diseased conditions, such as arteriosclerosis and hypertension, the vein frequently becomes indented when crossed by the artery, so that it shows a definite constriction and, at times, an apparent break in the regular course of the vessel.

RETINAL SIGNS OF AGING

With advancing years some fibrosis develops in the vessel walls. This is recognized by narrowing of their lumina, lessened translucency, and dulling of the light streak, especially of the arteries. This is not accompanied by any change in the regularity of the lumen of the vessels. Clinically, it is manifested by a general narrowing or attenuation of all the retinal vessels with little or no abnormal elevation of blood pres-

sure. The choroidal vessels usually participate in this change to a certain degree, frequently recognized through the thinning retina of senility. If advanced arteriosclerotic changes develop, sclerosis of the choroidal vessels is strikingly visible through the ophthalmoscope as a white interlacing pattern bordering the pale pink outline of the vessels.

DRUSEN

Another rather common change in the retina of people of advanced years is known as *drusen*. These appear as small round or oval dots of a yellowish-gray (sometimes a light pink) color scattered over the fundus. At times they become quite prominent and may be lighter in color, surrounded by a more densely pigmented halo.

Anatomically drusen consist of small discrete elevations on the lamina vitrea of the choroid, just beneath the pigment epithelium. They are made up of a colloid material produced by some abnormal or excessive secretory action of the pigment epithelium, which is it-

self displaced by the substance as it accumulates. These drusen bodies or colloid deposits may at times be few in number, or they may be numerous. They are considered a normal accompaniment of senescence, and as a rule produce no defect in vision unless they are massed in the macular area, in which case a considerable reduction in central vision may follow. Occasionally they are seen in young people.

SENILE MACULAR DEGENERATION

SENILE degeneration of the macula is relatively common in the aged and is associated with arteriosclerosis. The ophthalmoscope may show anything from a few scattered pigment dots to widespread degeneration in the macular and perimacular area. The remainder of the retina may appear essentially normal, aside from thinning and some signs of sclerosis of the choroidal and retinal vessels.

The macular degeneration arises from sclerosis of the choroidal vessels, particularly the choriocapillaris immediately beneath the macula. A reduction in central visual acuity, which may be profound, may be the only symptom for a considerable period, since involvement of the periphery of the choroid and retina may be slight or absent for some time.

ARTERIOSCLEROSIS AND HYPERTENSION

Ophthalmoscopic examination can be an important aid in the diagnosis of generalized arteriosclerosis and hypertension. It should be remembered, however, that the retinal vessels are but a localized area of the blood vascular system and they may not always depict the status of the vessels throughout the body. Duke-Elder stresses the well-known fact that vascular sclerosis of various types is rarely uniform, at one time being predominantly ocular, at other times cardiac, cerebral, or renal. However, statistics from many observers reveal a high incidence of retinal arteriosclerosis in generalized arteriosclerosis, varying from 40 per cent to 80 per cent. A similar situation is revealed in hypertension. Wagner reports 56.6 per cent retinal arteriosclerosis in 200 cases of hypertension, though generalized arteriosclerosis was

not evident in 30 per cent of the patients showing retinal arteriosclerosis. Of the 200 cases 46.5 per cent showed general disease, but 20.4 per cent of these showed no retinal involvement, and 13.5 per cent had cerebral arteriosclerosis though no retinal changes were associated in 25.9 per cent of these.

Thus it will be seen that arteriosclerosis is a "capricious disease," as so aptly phrased by Duke-Elder in his masterly discussion of various phases of this complicated subject, "varying much in the extent of its manifestations all over the body, but most authors are agreed that *arteriolar sclerosis* is distributed regularly with great uniformity throughout all the organs. Moreover, while retinal sclerosis can give no safe indication of the *degree* of sclerosis elsewhere, its occurrence in the eye almost certainly indicates its presence generally."

Arteriosclerosis of the retinal vessels is manifested not alone by extreme narrowing of the vessels but also by changes in color of the vessels. The light streak of the artery may become extremely bright due to the increased reflection of light from the thickened medial coat of the vessel wall, which may finally advance to a state of hyaline degeneration at which point the color of the reflex takes on a coppery hue; they are then commonly described as "copper wire arteries." As the sclerosing process increases, the thickened walls of the arteries become more visible, and the vessels assume a silvery-white hue and are designated "silver wire arteries." Periarterial fibrosis may be added to this, occasionally producing "pipe-stem arteries," so called because of the encircling white coating. This is regarded by some investigators as evidence of previous retinitis in these areas. Irregularities in the lumen of the arteries may develop as a result of thickening of the vessel walls.

The finer terminal arterial twigs may become extremely tortuous, resembling a corkscrew. This may be particularly noticeable in the perimacular areas, where the small terminal branches point toward the macula, a condition well described by de Schweinitz. When the arteriosclerotic process is advanced, areas of

localized ischemia may develop in the retina, with resultant degenerative areas recognized ophthalmoscopically as small white "hard" spots, usually in the deeper layers of the retina in the central area. Small hemorrhages may also develop, appearing striate or flame-shaped when they lie in the superficial layers of the retina, or round and sharply defined when confined to the deeper layers.

THESE changes may be bilateral or unilateral and may remain unchanged for long periods of time, according to Foster Moore, who has furnished the most complete and thorough description of the condition. These changes have been designated "arteriosclerotic retinitis" by him. The disease runs a relatively benign course. Since an associated hypertension of varying degree may develop in the course of the disease, some authors attribute many of the changes observed to this and question the validity of Foster Moore's contention that the condition is primarily an arteriosclerotic process. However, it is seen quite frequently and does not have the characteristics of essential hypertension either from an ophthalmoscopic or from a general clinical standpoint. I have seen retinal changes of this type in the aged, whose blood pressure had never been elevated beyond that considered normal for their age group.

OCCLUSION OF THE CENTRAL ARTERY AND VENOUS THROMBOSIS

Occlusion of the central retinal artery by embolism or thrombosis may develop in the course of retinal arteriosclerosis, though other diseases may be a contributing factor. It is recognized by generalized pallor of the retina due to ischemia, marked constriction or disappearance of the retinal arteries, and the well-known cherry-red spot at the macula. The macula appears red due to the presence of the underlying choriocapillaris by which it is nourished, and it is, therefore, not affected by the retinal edema incident to the occlusion of the retinal artery.

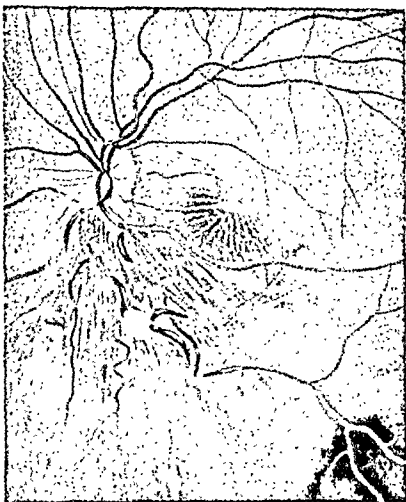


Figure 28. Thrombosis of a branch of the central retinal vein (from Duke-Elder, after Parsons, *Textbook of Ophthalmology*; C. V. Mosby Co., 1940-41).

Thrombosis of the central retinal vein or of one of its branches may also develop in arteriosclerosis, especially when some added toxic factor is superimposed. Thrombosis of one of the branches of the main vein frequently occurs at a point of arteriovenous crossing when the vein has previously suffered some damage from constriction due to sclerosis of the adjacent artery or fibrosis in the connective tissue septa common to the vein and artery. These conditions, while frequently disastrous from a visual standpoint, usually are not of immediately grave prognostic significance so far as life is concerned, for many patients live for years after the vascular accident.

The ophthalmoscopic picture is quite characteristic and easily recognized. When the main central vein is involved, massive hemorrhages are seen scattered throughout the retina. The veins are much engorged and tortuous; the arteries are unaffected, though at times ob-

scured by accompanying retinal edema. White patches later appear in the retina, and at times a star-shaped figure may develop in the macula. In branch-thrombosis a similar picture is seen, limited to the area involved. Frequently the site of the rupture of the vein can be seen, usually at the point of an arteriovenous crossing.

DIABETIC RETINOPATHY

A retinitis (retinopathy) similar to that described as "arteriosclerotic retinitis" occasionally develops in diabetics. The ophthalmoscopic appearance is quite characteristic, consisting of small round or oval white degenerative spots, or so-called exudates, which lie in the deeper layers of the retina. Numerous hemorrhages, typically round or punctate, are scattered throughout the retina, chiefly in the central area. They may precede the development of exudates for a considerable period of time. They are sharply delimited as a rule, owing to their position in the deeper layers. Sometimes the white dots assume a circinate arrangement surrounding the macula when somewhat larger globular white areas become confluent.

There is still some controversy as to the pathogenesis of the retinal changes associated with diabetes, with some authorities contending that they are the result of arteriosclerotic changes which so commonly occur in diabetes. However, since typical diabetic retinopathy appears at times in young subjects who show no evidence of arteriosclerosis, the retinal changes are regarded by many observers as a distinct clinical entity which arises from metabolic disturbance incident to the diabetes. At times an associated hypertension may serve to complicate the typical retinal changes which are so characteristic of the disease.

HYPERTENSION

The fundus changes which are associated with various types of hypertension have assumed considerable importance in recent years due to the advance in our knowledge of this disease. The retinal changes which occur in arteriosclerosis and renal disease have been

long known, and their grave prognostic importance in certain forms of kidney disease have been generally recognized.

Only in comparatively recent years has the hypertension per se, whatever may be its cause, assumed the major role which it is now accorded in the evaluation of cardiovascular-renal diseases. At the present time many authorities attribute the varied retinal changes, which at times accompany these diseases, solely to the associated hypertension.

ELWYN, in an article concerning the various fundus changes which may be observed in hypertension, has admirably summarized the basic conditions which may at times be responsible for the rise in blood pressure. I submit this summary in a somewhat abbreviated form.

FORMS OF HYPERTENSION (from Elwyn)

- I. Essential hypertension—benign phase
- II. Malignant renal sclerosis, or the malignant phase of essential hypertension
- III. Hypertension of renal origin
 - A. Diffuse glomerulonephritis (acute, subacute, subchronic, and chronic)
 - B. Rare forms of renal disease
 1. Amyloid kidney
 2. Unilateral renal hypoplasia
 3. Polycystic kidney
 4. Periarthritis nodosa with renal vascular changes
 5. Hydronephrosis
 6. Pyelonephritis
 7. Prostatic obstruction
- IV. Hypertension of pre-eclampsia and eclampsia of pregnancy
- V. Hypertension accompanying tumors of adrenal glands and basophilic adenoma of the pituitary gland (Cushing's syndrome)

It is evident from this classification that hypertension may occur in a variety of conditions. The subject is too extensive to attempt a description here of the varied retinal changes which may develop in the course of all of these diseases. Volhard, Fishberg, Wagener, and many others emphasize the importance of the hypertension per se, as the basic cause of the retinal changes which are encountered whether it is of essential, renal, or toxic origin. It may be seen, therefore, that at times a similar re-

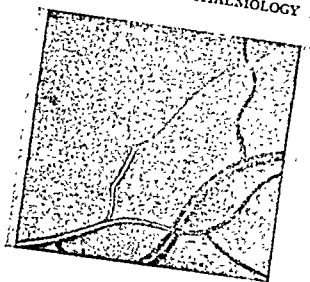


Figure 29J. Spasm of artery (from Gipner, John F., *The Clinical Significance of Retinal Arterial Changes and Retinitis in Cardiovascular Renal Disease*; New York State J. Med., August 1930). Artery: normal or sclerosed. Vein: normal. Caliber of artery: constricted at point of spasm. Lumen of artery: obliterated at point of spasm. Peripheral branches of artery: reduced to threads or invisible.

tinal picture may evolve in a variety of general conditions in which hypertension is the dominant characteristic. Differentiation or separation of some of these is therefore difficult and, at times, impossible.

Since the kidney is frequently involved, early or late, in most of these conditions, the retinal changes were formerly attributed to the associated albuminuria. Now it is well known that albuminuria has nothing to do with the retinal changes, so the old familiar term "albuminuric retinitis" has been discarded for the term "hypertensive neuroretinopathy." The latter is more descriptive since it indicates that the disease process arises from hypertension and that the retinal changes are degenerative rather than inflammatory in character. Because of limited space I shall confine my discussion of this subject to the retinal changes associated with so-called essential hypertension since they are by far more frequently encountered and, therefore, are of greater interest to the clinician and ophthalmologist alike.

ESSENTIAL HYPERTENSION

In defining the term "essential hypertension," Fishberg states, "the concept of essential hypertension includes those cases of chronic hypertension which neither clinically nor

anatomically can be demonstrated to have evolved from antecedent inflammatory disease or urinary obstruction." This author, however, admits the definition is defective and further states "the very term 'essential hypertension' is a confession of ignorance and this is its chief virtue."

Duke-Elder gives a somewhat wider scope to his definition, viz., "Essential hypertension is a persistent and usually progressive raising of the blood pressure which represents the response of the vascular system generally to some underlying disorder, hereditary, metabolic, toxic, infective, endocrine, or psychological, which probably causes primarily an overactivity of the vasomotor center by nervous or chemical presor agencies."

A SATISFACTORY classification of the retinal changes observed in essential hypertension is difficult to offer since neither ophthalmologists nor clinicians agree concerning either the pathogenesis or the terminology of the disease. Likewise, description of the vascular changes encountered in retinal vessels vary with practically every writer on the subject. It is my purpose merely to point out certain commonly recognized signs in the retina and retinal vessels which may aid the general practitioner in establishing a diagnosis and following the progress of the disease.

The terms "benign" and "malignant hypertension" have been fairly generally used by some authors, particularly Keith and Wagener, though they are by no means universally adopted by all writers. The term "benign hypertension" refers to cases of persistent elevation of blood pressure which may extend over a period of many years and which may be, in the earlier phases, accompanied by few if any general symptoms and by virtually no visible changes in the fundus oculi.

Therefore, for a considerable period in the course of benign essential hypertension the retinal vessels appear normal, and ophthalmoscopic examination would be of assistance only for its negative value (Elfwyn). Unless blood

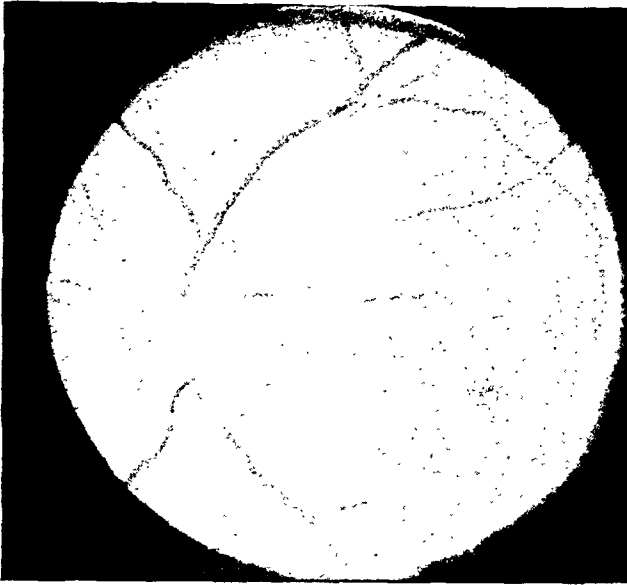


Figure 29b. Diffuse vasospasm of retinal arteries in hypertension (Grade II) (Author's case). Blood pressure 216/126. Urine negative.

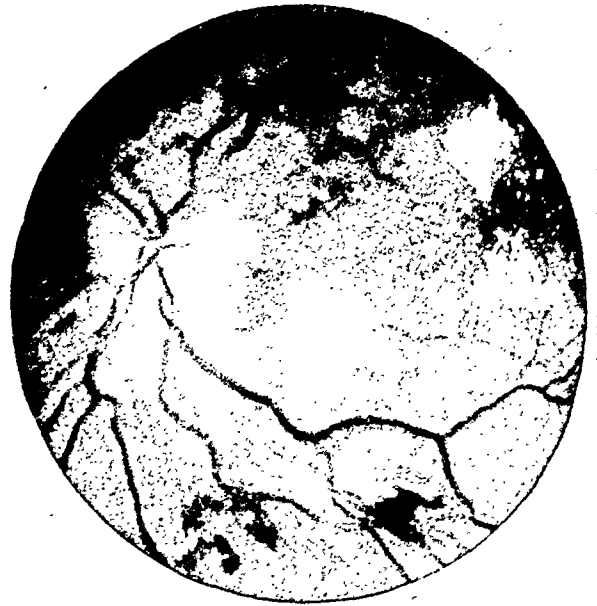


Figure 31. Retinitis of malignant hypertension (third stage) (from Lillie, Cardiovascular Renal Disease; D. Appleton-Century Co.). Note extensive edema of disk; marked attenuation of arteries; numerous hemorrhages and exudates.

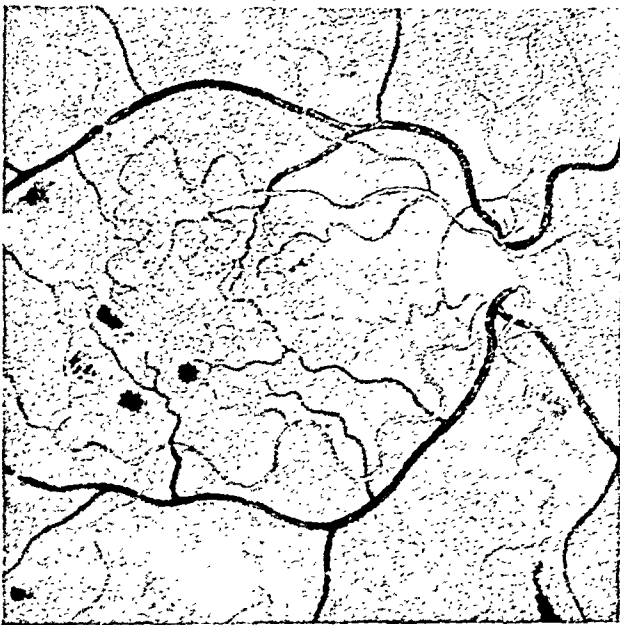


Figure 30. Retinitis of hypertension (severe benign type of Wagener) (from Gipner, John F., The Clinical Significance of Retinal Arterial Changes and Retinitis in Cardiovascular Renal Disease; New York State J. Med., August 1930). Arteriosclerosis of hypertension type; diffuse narrowing of arteries; exaggerated reflex; irregularities in caliber of terminal vessels; arteriovenous compression; cotton-wool patches; scattered hemorrhages.

pressure readings are made by the ophthalmologist as well as by the clinician, many of these cases will be overlooked.

In the later stages of benign hypertension important signs appear in the retina. These evidently are a result of wear and tear on the retinal vessels caused by the persistent hypertension which thereby induces varying degrees of vascular sclerosis. One of the most common signs encountered is narrowing of the arteries and indentation or deviation of the veins at arteriovenous crossings. Arteriovenous compression, or variations of it, may arise from many different pathologic changes in and adjacent to the artery. Fishberg states that it may be present at times without arteriosclerosis, especially in hypertension of recent or acute origin, such as is seen in toxemia of pregnancy and acute glomerulonephritis, when venous compression may be attributed to the increased rigidity of the overlying artery owing to turgidity incident to the increased blood pressure. This is sometimes called "Salus' sign," since he made some very thorough studies of it.



Figure 32a. Malignant neuroretinopathy (author's case). Photographs of the fundus of a patient with malignant hypertension (female aged 40; kidney function excellent; blood pressure 240/136). Note edema of the disk and retina; marked spasm of the retinal arteries; tortuosity of the terminal vessels; numerous hemorrhages and exudates; beginning star-shaped figure in the macula.

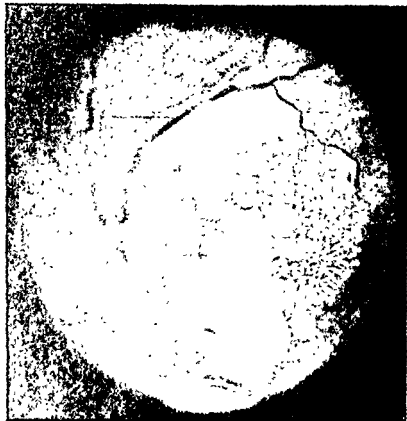


Figure 32b. Malignant neuroretinopathy (author's case). Photographs of the fundus of a patient with malignant hypertension (female aged 40; kidney function excellent; blood pressure 240/136). Note edema of the disk and retina; marked spasm of the retinal arteries; tortuosity of the terminal vessels; numerous hemorrhages and exudates; star-shaped figure in the macula, more advanced stage.

Most authors consider arteriovenous compression merely as evidence of sclerosis in the vessel walls which has been brought about by the persistent hypertension; it is, therefore, included under the heading "arteriosclerosis" in some classifications of the disease. In my experience, arteriovenous compression and variations of it are constantly seen in early hypertension. I seldom have failed to find a considerable elevation of blood pressure when its presence is marked. As a rule, the diastolic pressure is usually disproportionately elevated, recordings of 90 to 100 being quite common. Generalized narrowing of the retinal arteries is usually also present, and later, when the process is more advanced, irregularity in the caliber of certain vessels may appear. This condition apparently may remain relatively stationary for a considerable period of time, or it may gradually progress.

Usually if we are dealing with a true malignant type of hypertension, the retinal vessels show a generalized vasospastic contraction (see Fig. 27-c), variously described as angiospasm, arteriospasm, vasospasm, etc., with marked increase in blood pressure. The spasm may be localized but is more frequently diffuse, involving most of the arteries. The diastolic pressure assumes major importance and it may be found in the range of 110 to 120. Later, if the spastic contraction persists for any length of time, changes appear in the retina proper, such as localized areas of edema, to be followed still later by white cotton-wool patches and hemorrhages of various types. Varying degrees of vascular sclerosis usually appear. This picture represents further progression of the disease process and is of much graver prognostic significance.

This stage of the disease has been described

by Wagener and associates as "severe benign" type, since he has found that, although of a serious nature, many of these cases may improve with appropriate general treatment, and the retinal changes may also clear up in part. The hemorrhages and exudates absorb, and the spastic contraction in the arteries subsides. The patient is generally improved. Blood pressure, however, remains elevated, and similar recurrent episodes may develop with final progression of the disease until the characteristic picture known as "malignant hypertensive neuroretinopathy" appears.

THE retinal changes in this condition are quite characteristic. There is a swelling of the nerve head and surrounding retina due to edema, with numerous hemorrhages and white patches scattered over the fundus. The white spots are of two types—cotton-wool patches, and more sharply defined, glistening deposits, especially in the deeper layers of the retina and, at times, in the macular area, where they may assume the form of star-shaped striae or fan-like figures. The fluffy, soft, cotton-wool patches are produced in part by degeneration of the nerve fibers resulting from the ischemia which follows extreme vasospasm, recognized microscopically as cytoid bodies (Grear), and also by transudates of serum and precipitated fibrin in the deep retinal layers. The "hard" white spots and the white striae in the macula consist of masses of fat-laden cells, sometimes called bladder cells or "histocytes" (Grear). They are frequently referred to as "edema absorbing exudates" (Wagener).

Some authors claim this malignant phase of essential hypertension is, indeed, a separate clinical entity and, therefore, does not arise from a pre-benign process; other authorities state it may be the terminal phase of a long-standing benign type of hypertension. The disease is more common in the younger age group, from 30 to 50. Certainly such forms, as those seen in the toxemia of pregnancy, develop rapidly, and frequently there has been no antecedent hypertension or arteriosclerosis. I have

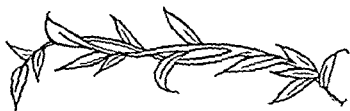
frequently seen the disease in young people under 30.

The retinal vessels show marked constriction of the arteries and some branches may be reduced to mere threads. Frequently there is marked irregularity in the caliber of the vessels with alternate dilatation and constriction. Many of the finer vessels may be completely obscured by the intense retinal edema. The terminal branches of both arteries and veins are frequently tortuous. The blood pressure is usually very high, ranging from 200 to 290 systolic and from 130 to 160 diastolic, or higher. This fundus picture is of extremely grave significance, and few patients survive longer than a year or two after its appearance.

The various retinal changes described above may be conveniently classified as Grades I to IV, depending upon the extent and severity of the lesions encountered. In the absence of any general agreement concerning the classification of the sclerotic and spastic changes which appear in the vessels in hypertensive vascular retinal disease, the rough method of grading the degree of sclerosis I to IV, and spasm in stages I to IV has been found expedient.

The fundus changes in the toxemia of pregnancy and in some cases of chronic parenchymatous nephritis may be indistinguishable from those of malignant hypertension. It is now generally conceded that the severe hypertension which is also present in certain stages of these diseases is responsible for the retinal changes, so the retinal changes are the same for practical purposes though there may be some variations in the fundus picture recognizable by one expert in ophthalmoscopic interpretation. If there has been a pre-existing sclerosis of the retinal vessels of long standing, varying grades of this may be present and afford some information as to the duration of the disease process.

The writer has freely drawn upon various well known standard texts and atlases in the preparation of parts of this paper. The textbooks and atlases of C. Adam and of Axenfeld, and the more recent text of W. S. Duke-Elder have been found invaluable and are recommended to the student who wishes more complete information regarding this subject.



Roentgenologic Diagnosis of Diaphragmatic Hernia

B. R. KIRKLIN*

MAYO CLINIC, ROCHESTER

THE DIAGNOSIS of diaphragmatic hernia, broadly speaking, is essentially a roentgenologic problem. At the Mayo Clinic, 90 per cent of these hernias are found more or less unexpectedly at routine examinations of the stomach, or more rarely of the colon, to determine the cause of gastrointestinal symptoms. In the remaining 10 per cent of cases the patient comes with the diagnosis already made, or the clinical history is suggestive of hernia, or routine roentgenograms of the thorax reveal abnormalities that may be due to hernia and so call for further roentgenologic investigation.

In all roentgenologic examinations of the stomach the possible existence of diaphragmatic hernia should be kept in mind by the examiner, and his standard technic should provide for that contingency. Since a vast majority of hernias are at the esophageal hiatus, the region of the esophagogastric juncture should invariably be inspected thoroughly while the first two or three swallows of the barium suspension are being taken. Displacement or hooklike curvature or angulation of the lower portion of the esophagus is suggestive of hernia and is a common manifestation. Retardation of the barium stream at the hiatus, disparity between the upper level

of the gastric contents and the site of the esophageal aperture, or what seems to be a high hourglass deformity should always make the examiner think of hernia. Any deviation from the normal size, contour, or general appearance of the lower part of the esophagus or any deviation from its normal relation with the stomach should cause the examiner strongly to suspect hernia and to demand further *roentgenoscopic* and *roentgenographic* study with the patient recumbent and strongly tensing his abdominal muscles. This technic is necessary to confirm the presence, and to demonstrate the extent, of herniation. Hernia in which only the colon or small bowel is implicated cannot be confirmed definitely or excluded confidently without employing the barium enema or observing the transit of the barium meal.

Roentgenologic manifestations of diaphragmatic hernia vary with the site of the lesion, the abdominal viscus extruded, and with the extent of extrusion. These factors in turn are related to other factors, such as the anatomy of the region involved and the cause of the hernia.

As might be expected, many classifications of hernia have been offered, almost as many as there are writers on the subject. Harrington¹ has proposed what seems to me to be the most complete and practicable classification of all,

*Section on Roentgenology.



B. R. KIRKLIN

for it can be applied satisfactorily by the surgeon, the clinician, and the roentgenologist. Items in this classification that are of roentgenologic significance are as follows:

1. Hernia through the esophageal hiatus
 - a. Congenitally short esophagus with thoracic stomach
 - b. Esophageal hiatal hernia with shortened esophagus
 - c. Esophageal hiatal hernia without shortening of the esophagus
 - d. Para-esophageal hernia through the hiatus
2. Hernia through the foramen of Morgagni
3. Pleuroperitoneal hernia
4. Hernia through congenital defects in the diaphragm
5. Congenital absence of the hemidiaphragm
6. Posttraumatic hernia

HERNIAS THROUGH THE ESOPHAGEAL HIATUS

These constitute 98 per cent of the diaphragmatic hernias and are found at more than 1 per

cent of all roentgenologic examinations of the stomach at the Mayo Clinic.

Congenitally short esophagus with thoracic stomach—This is a rare variety. In this type the esophagus is short and straight and the stomach is not truly herniated, since the supradiaphragmatic portion has never been below the diaphragm. In the single case seen at the clinic, five-sixths of the stomach was located above the diaphragm, and the hiatus was 12 cm. in diameter. The roentgenologic diagnosis of hernia should be self-evident in most cases; if the esophagus is extremely short it may fairly be assumed that the condition is congenital, but in less pronounced instances distinction from the next variety to be discussed is scarcely possible.

Esophageal hiatal hernia with shortened esophagus—This designation is intended to imply that originally the esophagus was of normal length but that it became shortened by tonic contraction following the hernia and that the term "thoracic stomach" does not apply. At operation the surgeon can base this diagnosis on the fact that the esophagus can be stretched to approximately its normal length. Of course the roentgenologist cannot determine whether such elasticity exists or not, but he will incline toward this tentative diagnosis because a large proportion of the hiatal hernias are of this variety, and the true short-esophagus thoracic-stomach variety is exceedingly rare.

Esophageal hiatal hernia without shortening of the esophagus—This term is chosen to designate those hernias in which the esophagogastric juncture is above the diaphragm, and the lower end of the esophagus is slightly or markedly redundant, a feature which distinguishes the group from the hernias with shortened esophagus. It is the most common type of hiatal hernia, and 66.5 per cent of the hiatal hernias observed roentgenologically at the clinic in 1944 were of this variety.

Para-esophageal hernia through the hiatus—This term designates a variety of hernia in which a portion of the stomach is extruded through the esophageal hiatus, but the esophagogastric junction remains below the diaphragm and the esophagus does not participate

in the hernia. Any part of the stomach may be involved, but most often the cardia is implicated. This group is small, constituting only 7.5 per cent of the hiatal hernias examined roentgenologically at the clinic in 1944.

IN EFFECTING the roentgenologic diagnosis of esophageal hiatal hernia and distinguishing among its varieties, certain items are of fundamental importance. First, the basic point of orientation in the diagnosis is the exact situation of the esophagogastric junction in relation to the diaphragm. Second, retardation of the barium stream at the hiatus is highly significant of hernia, for it occurs in almost all cases. Third, redundancy and tortuosity of the lower portion of the esophagus without dilatation is strongly suggestive of hernia, for it is present in more than one third of the cases.

Many technics have been devised for the demonstration of hiatal hernias. Satisfactory inspection of the esophagogastric juncture and its vicinity can usually be obtained in the customary anterior view with the patient standing. Then, as he takes the first swallows of the barium mixture, he should be required to strain his abdominal muscles in order to reproduce any hernia that may have been reduced. Pressure of the examiner's hand over the patient's stomach may also elicit such hernias. If these measures give negative results and doubt persists, roentgenograms should be made with the patient lying on his back and tensing his abdominal muscles.

HERNIA THROUGH THE FORAMEN OF MORGAGNI

This type of hernia, also termed "parasternal" or "costosternal" hernia, is quite uncommon. The so-called foramen is a bilateral, retrosternal, triangular space bounded in front by the sternum, medially by the sternal portion of the diaphragm, and laterally by the costal portion of the diaphragm. The hernia may be unilateral or bilateral, and either stomach or colon, or both, may be implicated. Occasionally only the omentum is involved. First evidence of the

hernia is likely to consist of abnormal shadows near the midline and at the base of roentgenograms of the thorax. Lateral roentgenograms may reveal fluid and gas in the contents of the hernia, and such findings are strongly suggestive. Examination with the aid of the barium meal, or with the aid of the barium enema, since the colon is involved more often than the stomach, may establish the diagnosis.

PLEUROPERITONEAL HERNIA

This type of hernia, or hernia through the foramen of Bochdalek, is one located through a posterior segment of the diaphragm, a weak spot and point of fusion in the development of the organ. These hernias are congenital. Harrington has estimated that 75 per cent of infants with this condition die shortly after birth; few of the remainder reach adulthood. Bizarre shadows in the thorax are likely to be the first clue to the condition, and roentgenologic examination of the stomach, small bowel, and colon may lead to the diagnosis.

HERNIA THROUGH CONGENITAL DEFECTS IN THE DIAPHRAGM

These hernias, other than those through the foramen of Morgagni or Bochdalek, have been found most often in infants and children. Usually the hernia is through the left half of the diaphragm, and the stomach, colon, small bowel, or spleen may be implicated. Abnormal shadows at the base of the lung, especially on the left, in roentgenograms of the thorax are usually the first observed significant manifestations and call for examination of the alimentary canal with the aid of opaque media.

CONGENITAL ABSENCE OF THE HEMIDIAPHRAGM

Displacement of abdominal viscera into the thorax resulting from congenital absence of a hemidiaphragm is rare. Usually it is the left half of the diaphragm that is wanting. Roentgenograms of the thorax show striking abnormality of the affected side, and the presence of

the gas bubble or colonic haustra may indicate that the stomach or colon is in the thoracic cavity. However, administration of the barium meal or enema may be necessary to identify such displacement. In any case, the condition must be distinguished from other varieties of hernia and from eventration.

An exceedingly rare variety of congenital hernia is that resulting from congenital peritoneopericardial defect with herniation of abdominal viscera into the pericardial sac. A case has recently been reported by Wilson, Rumel, and Ross,² who have found only 8 similar cases recorded in the literature.

POSTTRAUMATIC HERNIA

Posttraumatic hernia may result from wounds by weapons or missiles, from crushing injury or violent forward flexion of the body, or from localized erosion or inflammatory necrosis of a segment of the diaphragm. Any portion of the diaphragm may be penetrated. Roentgenograms of the thorax constitute a common approach to the discovery and diagnosis of these hernias by disclosing abnormal shadows extending upward from the bases of the lungs. Occasionally the presence of the stomach or colon in the hernia is apparent, but complete and confident diagnosis requires examination with the aid of the opaque meal and enema. If only a solid viscus,

such as the liver or the spleen, is implicated, diagnosis may be difficult.

COMMENT

Obviously, the roentgenologic diagnosis of diaphragmatic hernia depends on demonstrating the presence of part or all of an abdominal viscus above the diaphragm, or proving the existence of an aperture in the diaphragm through which an abdominal viscus can be extruded by an increase of the intra-abdominal pressure. In any case, the position of the diaphragm must be ascertained by tracing its curvilinear shadow, and this may be difficult in cases of gross traumatic rupture. In an overwhelming preponderance of cases the stomach or bowel participates in the hernia, and this fact can be established by administering a radiopaque meal or enema. In all such instances the differential diagnosis is evident. If, however, the hernial content consists of a solid viscus only, such as the spleen or omentum, the lesion is likely to be mistaken for a neoplasm at the base of the lung, though if the hernia is reducible the diagnosis should be evident. Distinction of several varieties of hernia from one another can usually be made. Many hernias will escape discovery unless the roentgenologist keeps the condition in mind at every examination of the thorax and of the alimentary canal.

REFERENCES

1. HARRINGTON, S. W.: Diagnosis and treatment of various types of diaphragmatic hernia. *Am. J. Surg.* 50:381-446 (November) 1940.
2. WILSON, A. K., RUMEL, W. R., and ROSS, O. L.: Peritoneopericardial diaphragmatic hernia. *Am. J. Roentgenol.* 57:42-49 (January) 1947.

DIAGNOSTIC CLINIC

Treatment of Psoriasis

CLINTON W. LANE*

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

PSORIASIS is an acute, more often chronic, dermatosis originating as small, bright red papules, which rapidly or slowly increase in size to form raised, flat-topped disks or plaques of varying size and shape usually covered with dry, adherent scales. It has a predilection for the knees, elbows, and scalp, but the eruption may become generalized. At times the nails are involved. There is a seasonal variation with a majority of the exacerbations in the winter months. The general health is not usually affected except in those patients who have a complicating arthritis. The cause of the disease is unknown and treatment does not produce a permanent cure.

According to a statistical study,¹ psoriasis is one of the ten most common skin diseases, being eighth in incidence. It constitutes 6 per cent of all the skin diseases that are observed. It may occur at any age, the youngest reported case occurring in a baby six days old,² but ordinarily the disease begins in the second or third decade,³ most often between the ages of 15 and 30 years. Uncommonly it first appears

after the age of 45, but rarely past the age of 60. In a large series⁴ of cases the ages of the patients varied from 6 to 82 years and the longest duration of the disease on record is fifty-five years.

Psoriasis occurs as frequently in females as in males and in the Caucasian race equally in blondes and brunettes, but the disease is rare in the Negro and is almost unheard of in the full-blooded Negro. In the latter a biopsy should confirm the clinical diagnosis of psoriasis and a blood serology should be obtained, because the eruption may be the psoriasiform type of secondary syphilis.

Psoriasis is noninfectious and noncontagious, but there is a familial incidence in 25 to 40 per cent of the cases. This is a familial predisposition and not a dominant characteristic.

The disease is common in the Arctic and Temperate zones, but occurs less often in the Tropical zone; in Panama, Central America and Southern Europe psoriasis is seldom observed. In the United States psoriasis is observed more often in Missouri than in Louisiana or Texas, whereas Chicago, Minneapolis, and Boston have a great deal more psoriasis than does St. Louis. Likewise in the Temperate zone the disease is more prevalent in winter than in summer. Approximately 75 per cent of

*Assistant Professor of Clinical Dermatology, Washington University School of Medicine, St. Louis.

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the patients with psoriasis will develop recurrences or exacerbations of the eruption in cold weather, but will again improve with the onset of warmer weather in May and June. About 15 per cent claim there is no change with the seasons whereas 10 per cent state they are worse in the summer than in the winter.

The cause of psoriasis is unknown although numerous theories have been proposed. At present there are many advocates of the theory that a disturbed fat metabolism is the cause of the disease. Substantiating this opinion are the finding of a disturbed lipid metabolism by Grütz and Bürger,⁵ the observance of extracellular fat in the uninvolved skin of psoriasis patients by Madden,⁶ the beneficial effect of sarsaparilla (which has an affinity for cholesterol) by Deneke⁷ and Thurmon,⁸ of lipotropic substances such as soybean lecithin by Goldman⁹ and of lipocaic, a fat metabolizing pancreatic hormone by Stewart, Clark, Dragstedt and Becker.¹⁰

Becker¹¹ states that any factor resulting in mobilization of fats and lipoids from the tissues such as low fat intake, starvation, pregnancy and adrenal cortex will benefit psoriasis. Vitamins B, C, D and defatted wheat germ are essential to the metabolism of fats because they stimulate the function of the adrenal cortex.

Some investigators believe that a disturbed nervous mechanism causes psoriasis. Many psoriatics do have neurocirculatory instability and exacerbations have occurred following shock or prolonged nervous tension, indicating that the nervous system has an effect on the course of the disease. Trauma is a factor as evidenced by the presence of Köbner's phenomenon. This consists in the appearance of lesions of psoriasis in a scratch mark, but occurs only in the acute stage of the disease.

Others claim that psoriasis is an infection of mycotic, bacterial or virus origin. A type of rheumatoid arthritis, the so-called "psoriasis arthropatica," occurs in a small percentage of patients, usually after an acute exacerbation of a chronic psoriasis. It is thought to be due to absorption of toxic products into the system from the acute, disseminated lesions.

THE patient with psoriasis complains of few symptoms. In the acute outbreaks itching, smarting or burning may occur, but only a small percentage of patients in the chronic stages experience pruritus and then only of a mild degree. In thickened patches painful fissures may appear. The chief complaint is the embarrassment produced by the eruption, often curtailing activities such as athletic pursuits and pleasure-producing hobbies.

The earliest lesion of psoriasis is a pinhead sized papule of bright red color. The papules slowly or rapidly increase in size to form larger papules and nodules, which in turn coalesce to form plaques or patches. Some of the patches become quite large and may cover such a wide area as the entire surface of a leg or forearm. The earliest lesions are round or oval, but as they coalesce various shapes and forms are produced. By peripheral extension of the patches gyrate figures occur. Healing takes place by central clearing with a resultant ring form, having a paler, depressed midportion and elevated red margins. After the active lesion regresses there results a red or reddish-brown stain, which persists for a varying period of time and eventually disappears without scar formation.

The scale characteristic of the disease occurs in the earliest lesions and persists throughout. It is thick, silvery-white, mica or asbestos-like, adherent in the center and looser at the margins. When the scale is removed small bleeding points are revealed although they are not always visible to the naked eye.

The sites of predilection are the elbows, knees, the extensor surfaces of the forearms and legs, the scalp and the sacral region. The chest, abdomen, back, thighs and arms are frequently involved, but rarely the mid-face, fingers, toes and mucous membranes. In the acute stage and often in children the eruption is diffuse, but there may be a wide dissemination of the chronic lesions. Very infrequently, a pustular type of the disease occurs on the palms and soles. Most of the so-called cases of pustular psoriasis are in reality pustular bacterids as described by Andrews¹² or acrodermatitis perstans.

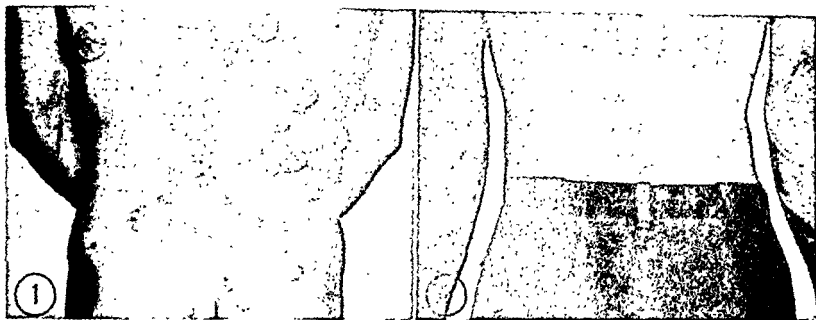


Figure 1. A chronic, discoid psoriasis. Plaques are covered with thick, adherent, silvery scales.

Figure 2. Scaly patches on the elbows, a common site for the lesions of psoriasis.

Figure 3. Extensive involvement of the anterior surfaces of the legs, another favorite site for the eruption. Scales have been removed by application of a keratolytic ointment.

Figure 4. Discrete patches of psoriasis in scalp margins.

Figure 5. Psoriasis nummularis of the trunk and intertriginous type of psoriasis in the axillae. Intertriginous type difficult to differentiate from seborrheic dermatitis.

Figure 6. Papular psoriasis of the abdomen and intertriginous psoriasis of the inframammary folds.



In chronic psoriasis there may be an involvement of finger and/or toenails in which the nails are of an opaque color with pitting, ridging and irregularity of the nail surfaces. The nail may separate at the base, may become raised from the nail bed by subungual scales and debris and finally may be destroyed.

An occasional complication is rheumatoid arthritis usually affecting the smaller joints of the hands and feet, the wrists and ankles, but also at times the larger elbow, knee, and shoulder joints. An odd occurrence in the experience of the author was the concomitant occurrence of rheumatoid arthritis in eight of the digits of the hands, which digits also revealed psoriasis of the nails, but the two digits without psoriatic nail involvement were also free of arthritis.

A disease which is difficult to differentiate from psoriasis is seborrheic dermatitis. Although both are prone to involve the scalp, the process is more uniform and diffuse in seborrhea. Likewise the eyebrows, mid-face and ears, sites where seborrhea most often occurs, are rarely involved by psoriasis. The color of the seborrheic eruption is yellowish-red as compared to the bright red of psoriasis and the scales are more loosely attached and greasier in seborrhea. In many cases it is difficult and at times impossible to differentiate between these two eruptions, particularly if the axillary, inframammary and crural regions are involved.

Pityriasis rosea involves chiefly the trunk, arms and thighs and rarely appears on the scalp or legs. The eruption is more acute, more evanescent, more pruritic than that of psoriasis and the scales are thinner. Typically the long axes of the macules of pityriasis rosea parallel the cleavage lines of the skin.

THE secondary eruption of early syphilis, particularly if it occurs in the Negro, may cause confusion in diagnosis. In the Caucasians the color of the secondary rash of syphilis is of a coppery-red shade as compared to the bright red of psoriasis. Also the scale is not as thick or adherent as in psoriasis and tends to form a

collarette at the periphery of the lesion. In both whites and Negroes the eruption of syphilis is arranged in circles or segments of circles in conformity to the vascular supply of the skin, while the palms, soles and face which are not frequently affected in psoriasis are often involved. Mucous membrane lesions, moist papules around mucocutaneous orifices, the general symptoms of headache, malaise, fever, the history of an initial lesion and the positive serology are all aids in differentiating syphilis from psoriasis.

Ringworm infection of the skin usually is manifested by macules or plaques with clearer, slightly depressed central portions and raised red margins. Such lesions resemble a regressing psoriasis, which tends to fade first in the central portion. The scale of a tinea eruption is less thick than that of psoriasis and the fungus can be demonstrated by direct examination of the scales or can be grown in a suitable culture medium. Ringworm infection of the scalp produces alopecia with broken hairs, a phenomenon which does not occur in psoriasis.

Nummular eczema of the extremities is more vesicular, more moist, more crusted and more pruritic than psoriasis.

The treatment of psoriasis cannot be successful unless the physician obtains the complete cooperation of the patient. An honest explanation should be made that although the present eruption can probably be eradicated, a promise of permanent cure cannot be made. Encouragement should be given by stating that the disease is not infectious, not contagious and almost never becomes malignant.

Many diets have been prescribed but all have been ineffective except the low fat diet, which has proved beneficial in some instances. Vitamins B, C, D and defatted wheat germ are of value because they are essential to the metabolism of fats. Sarsaparilla, which supposedly neutralizes the increased amount of cholesterol in the psoriatic is usually prescribed in the form of sas par tablets. They are well tolerated and are of value at times.

The drug which has been most effective in psoriasis is arsenic, administered as Fowler's

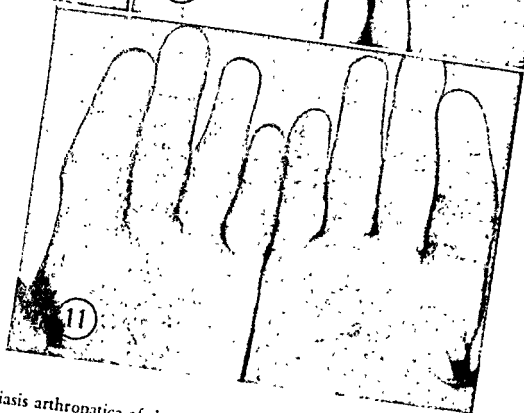
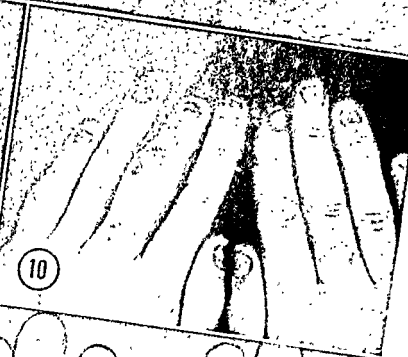
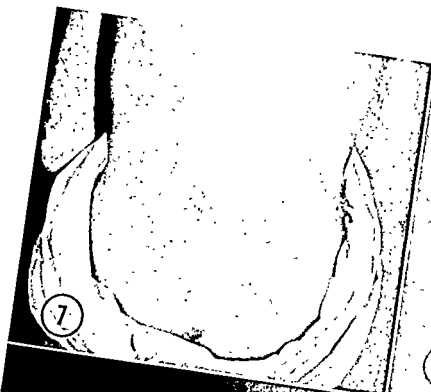


Figure 7. Psoriasis gyrata et figurata.

Figure 8. A rare manifestation of psoriasis on the mucous membrane of the penis. The red patches of psoriasis on the inner thighs resemble tinea cruris.

Figure 9. Psoriasis of the fingers, an area in which the disease seldom occurs.

Figure 10. Psoriasis of the nails with psoriasis arthropatica of the right third finger.

Figure 11. Pustular psoriasis of the palms.

solution (liquor potassi arsenitis). The daily dosage ranges from 6 drops at the onset with gradual increase to a maximum of 24 to 30 drops, normally given in divided doses. Symptoms of intolerance to the drug, such as eyelid edema, gastrointestinal cramps and diarrhea, necessitate a temporary discontinuance or a reduction in dosage. Arsenic should not be continued longer than ten or twelve weeks without a rest period because of its tendency to produce keratoses and carcinomas of the skin and its capability of inducing an exfoliative dermatitis. Furthermore, in a period of two to three months the success or failure of arsenical treatment can be determined. Arsenic trioxide in a dosage of $1/32$ to $1/16$ gr. three times daily, usually given as the Asiatic Pill is almost as efficient as Fowler's solution and often is better tolerated. Patients and pharmacists should be warned that prescriptions containing arsenic should not be refilled without the approval of the prescribing physician.

Autohemotherapy, which consists of the withdrawal of blood from the vein of the patient and immediate reinjection into the buttocks has been helpful on some occasions.

THE sulfonamide drugs, penicillin, and streptomycin are of no value in psoriasis. The salicylates may give relief from the pain of arthropathic psoriasis, but oddly the arthritis improves as the lesions of psoriasis fade and the arthritis becomes worse during an exacerbation of the eruption.

In the local management of the disease, bathing, which is often contraindicated in inflammatory skin eruptions, is of value because it removes the scales and thus permits the prescribed medicament to come in more intimate contact with the surface of the lesion.

Sunlight is an efficient therapeutic agent. Most patients with psoriasis obtain more relief in summer than in the winter and those areas exposed to the sun clear more rapidly. When sunlight is not available the ultraviolet light or the cold quartz light may be substituted although they are much less effective. However,

sunlight and ultraviolet light will often make an acute psoriasis worse and exposure to them should be avoided in the acute stages of the disease.

Liquor carbonis detergens, a mixture of coal tar and soap bark tincture, is the most valuable topical agent. Applied in full strength once or twice daily, it may be combined with exposure to sunlight or ultraviolet light, as tar, a photosensitizer, enhances the effect of these rays. Most patients tolerate the applications well and the rapidly drying solution is more pleasant to use than an ointment.

Chrysarobin, the standby of dermatologists for years, has the disadvantages of staining the skin, clothing, and bedding a brown color and of producing a severe conjunctivitis. This precludes its use on psoriasis of the scalp and face. Dihydroxyanthranol with the trade name of anthralin is a good substitute for chrysarobin. It is applied as an ointment varying in strength from 0.25 per cent to 2 per cent, does not stain as deeply or permanently as chrysarobin and can be applied to the scalp.

Other ointments which are helpful are those containing salicylic acid in 5 to 10 per cent strengths combined with ammoniated mercury or sulphur. These are particularly efficient in those eruptions which resemble seborrheic dermatitis.

Many patients, particularly women, object to the use of ointments on the scalp. For them the following lotion may be beneficial:

Rx Paraffin oil.....	140.0
Oleic acid.....	70.0
Oil of lavender.....	1.2
Phenol.....	1.2
$\frac{1}{2}$ of 1% sodium chloride	
water q.s.....	240.0

It also can be used on the glabrous occasionally will produce a ^{small} may be more irritating than folliculitis occurs the following substituted:

Rx Liquid petroxilin (N.F.).....	120.0
Phenol.....	1.2
Sodium chloride.....	1.2
Oil of lavender.....	0.2
Aqua destillata q.s.....	240.0

For solitary patches which have been resist-

ant to all treatment, x-ray therapy may be used. However, the number of previous roentgen exposures and the total dosage should be closely checked, because psoriasis will recur just as readily after x-ray treatment as after any other type of therapy. An individual is far better off with psoriasis alone than with psoriasis plus a severe radiation reaction.

REFERENCES

1. WRIGHT, C. S.: Newer treatment of common skin diseases. J. Michigan M. Soc. 42:105, 1943.
2. RILLE, J. Mal. Cut. 11:385, 1890.
3. ORMSBY, O. S., and MONTGOMERY, HAMILTON: Diseases of the skin. Philadelphia, Lea & Febiger, 1943, p. 278.
4. LANE, C. G., and CRAWFORD, G. M.: Psoriasis: statistical study of 231 cases. Arch. Dermat. & Syph. 35:1051, 1937.
5. GRUETZ, O., and BUEGER, M.: Psoriasis as a problem of metabolism. Klin. Wehnschr. 12:363 (March 11) 1933.
6. MADDEN, J. F.: Histologic studies of uninvolved skin of patients with psoriasis. Arch. Dermat. & Syph. 44:656-664 (October) 1941.
7. DENEKE, T.: General treatment of psoriasis. Deutsche med. Wehnschr. 62:337-341 (February 28) 1936.
8. THURMON, F. M.: Treatment of psoriasis with a sarsaparilla compound. New England J. Med. 227:128-133 (July 23) 1942.
9. GOLDMAN, LEON: Addition of lecithin to treatment routine in psoriasis: preliminary clinical report. Cincinnati J. Med. 23:166-170 (June) 1942.
10. STEWART, C. D., CLARK, D. E., DRAGSTEDT, L. R., and BECKER, S. W.: Experimental use of lipocain in treatment of psoriasis. J. Invest. Dermat. 2:219-230 (August) 1939.
11. BECKER, S. W., and OBERMAYER, M. E.: Modern dermatology and syphilology. Philadelphia, J. B. Lippincott Company, 1947, p. 231.
12. ANDREWS, G. C.: Diseases of the skin. Philadelphia, W. B. Saunders Company, 1946, pp. 262-263.



DAS NARRENSCHNEIDEN
By Pieter Brueghel (1556)

CASE REPORT

Congestive Splenomegaly With Cytopenia

SAUL FORTUNOFF

DESHON VETERANS ADMINISTRATION HOSPITAL, BUTLER, PENNSYLVANIA

CONGESTIVE splenomegaly with cytopenia has such varied clinical and laboratory manifestations that each case is worthy of study. In the case to be presented, all findings are in keeping with the above diagnosis and yet do not include all symptoms or signs listed in previously reported cases or in textbook descriptions of this illness. The response to splenectomy in this case was dramatic and encouraging in that a follow-up study at the end of a six-month period revealed sustained subjective and objective improvement.

CASE PRESENTATION

A 50-year-old white male was admitted to Deshon Veterans Administration Hospital in February 1947. At the time of admission the patient's complaints were diarrhea, pressure and pain in the abdomen, loss of weight, and extreme fatigue.

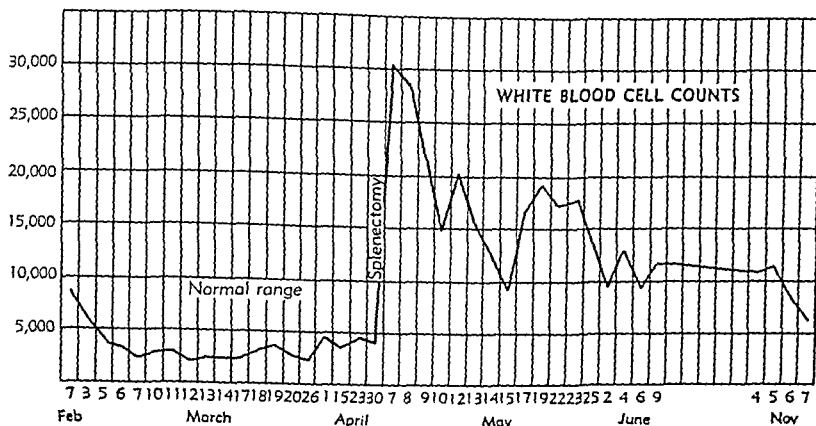
The patient was a veteran of World War I. Family history was negative except for diabetes in a sister and a cerebral accident as the cause of the father's death. This man was first hospitalized in 1922 for pleurisy and severe cough. A diagnosis

of tuberculosis was made, and from that time forward there were numerous hospitalizations for pneumonia and recurrent pulmonary hemorrhages. Approximately four years before admission this patient was hospitalized for pneumonia. During this latter hospitalization "a lump" was discovered in the abdomen. After complete x-ray studies, surgery for excision of "the lump" was recommended. The patient was not in favor of this procedure and so left the hospital against medical advice. In 1944 the patient was again hospitalized for pneumonia and since that time has been unwell.

The patient suffered from severe cough, weight loss, weakness and fatigue, and dyspnea on exertion. There was no history of ankle edema, orthopnea, or precordial pain. During the nine-month period before admission, the patient had eight to twelve loose stools daily. The stools were brownish in color and stringy in character. There was no history of melena or hematemesis. There were no periods of constipation. During this time the patient had a sensation of pressure and fullness in the upper abdomen which was aggravated by bending. Since November 1946 the abdomen had become swollen and the "lump" in the abdomen had become progressively enlarged. Because of the above signs and symptoms, hospitalization was recommended.

Physical examination revealed a bald-headed,

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Graph 1

white male of fifty years in no acute distress. Examination was essentially negative except for numerous coarse râles throughout the chest bilaterally. Râles were not constant in location and disappeared after diagnostic cough. Examination of the abdomen revealed two large masses. One was in the upper left quadrant and was free and movable and extended to a point below the level of the umbilicus and almost to the midline. The mass seemed notched at its inferior border. The other palpable mass was in the upper right quadrant and was rather rectangular in shape and did not extend to the right flank, but was palpable near the midline of the abdomen and extended for four finger-breadths below the right costal margin.

Because of the chest findings and history of previously active tuberculosis, the patient was studied to rule out active pulmonary tuberculosis. Six sputum examinations were negative for acid-fast bacilli, the patient was afebrile, there was a normal sedimentation rate and the chest x-ray was negative. After active pulmonary tuberculosis was ruled out, the patient was studied to determine the cause of his abdominal trouble.

Further questioning revealed that while the patient was hospitalized for pneumonia four years previously, he was treated with sulfadiazine and

it was found that he had a leukopenia and therapy was discontinued. After a lapse of ten days, however, the sulfa therapy was reinstated. Thus, the

TABLE I
BONE MARROW SMEAR, APRIL 17, 1947

Type of Cells	Per Cent Found	Per Cent Normal
Myelocytes	10.0	10-20
Neutrophils	9.0	
Eosinophils	1.0	
Juveniles	19.0	20-25
Stabs	17.0	5-10
Segmented	37.0	22.0
Neutrophils	34.0	20.0
Eosinophils	3.0	2.0
Lymphocytes	13.0	10-20
Monocytes	1.0	1-5
Megaloblasts	0.0	2.0
Erythroblasts	1.0	2-4
Normoblasts	6.0	22-35

Summary: Myeloid-erythroid ratio—13:1. No megakaryocytes seen. Depression of erythropoiesis.

Hematologic diagnosis: Hypoplastic anemia.

With the leukopenia and thrombocytopenia in this case, along with the anemia and presence of esophageal varices and a large mass in splenic region, we believe that this patient has Banti's disease. We feel that he is in the stage of the disease where the cirrhosis of the liver is far advanced and that he has been fortunate in not having any bleeding as yet, but bleeding may occur at any time. Suggest laparotomy with removal of the large mass which we feel is a Banti's spleen. (G. J. Brimley, M.D., pathologist.)



Figure 1. This roentgenogram shows depression and compression of the left kidney with kinking of the left ureter caused by the enlarged spleen.

first incidence of leukopenia occurred four years before admission. Frequent white counts were ordered after this information was obtained. (See Graph 1.)

Various x-ray studies were carried out:

1. A gastrointestinal series revealed that the stomach was displaced to the right. Also esophageal varicosities were discovered on fluoroscopy.

2. A barium enema showed that the splenic flexure of the colon was displaced to the right. The colon was normal.

3. An intravenous pyelogram showed that the left kidney was compressed and depressed by a mass in the upper left quadrant. The left ureter

was kinked.

4. Retrograde pyelogram confirmed findings of the intravenous pyelogram. (See Figure 1.)

Various liver function tests were done and yielded results that were within normal limits. (See Table 2.)

BECAUSE the platelet count was below normal and because there was a persistent leukopenia and normal differential count, a diagnosis of congestive splenomegaly with cytopenia was made. This diagnosis was made despite the absence of a severe anemia. (See Graph 2.) Bone marrow

TABLE 2
LIVER FUNCTION TESTS

	Preoperative	Postoperative
Total protein and A/G ratio		
Total protein (in gm.)	7.16	7.52
Albumin (in gm.)	4.37	4.22
Globulin (in gm.)	2.79	3.30
A/G ratio	1.6/1	1.1/1
Cephalin Flocculation test		
24 hours	1 plus	2 plus
48 hours	1 plus	3 plus
Bromsulfalein (5 mgm. per kilo of body weight)	6.3% recovery in 45 minutes	11% recovery in 45 minutes
Serum bilirubin (mgm.)	0.28	0.78
Prothrombin time (per cent)	100	100
Ratio of cholesterol esters (per cent)	41	75
Icteric index	6 units	8 units

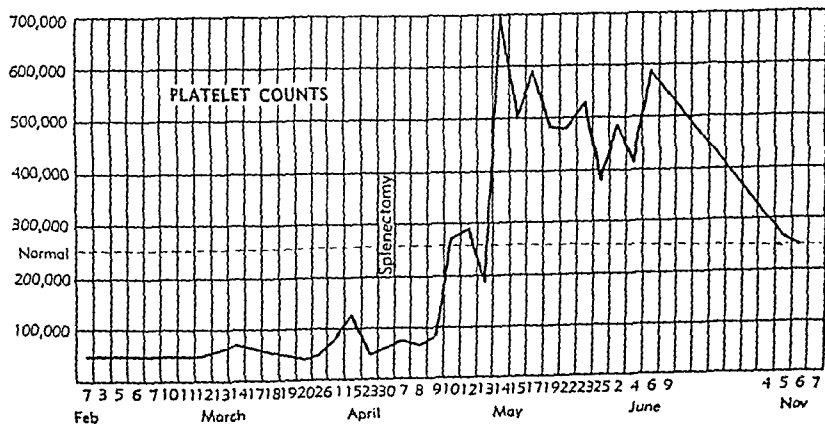
merous adhesions and after delivery of the spleen, the splenic pedicle was visualized. The vessels of the pedicle were extremely large and veins tortuous. Palpation of the liver by the surgeon revealed no gross hepatic pathology, but the left lobe was slightly enlarged. There were no signs of stenosis of the splenic vein or of other obstructive phenomena in the portal system. The patient made an uneventful postoperative recovery, and laboratory studies made postoperatively revealed some interesting findings. (See Table 2 and Graphs 1, 2, and 3.)

PATHOLOGIC REPORT ON THE SPLEEN

smear (sternal puncture) revealed depression of erythropoiesis with a myeloid-erythroid ratio of 13:1. (See Table 1.)

Surgical consultation was requested, and splenectomy was recommended. On May 6, 1947, an abdominal exploration and splenectomy was performed by one of us (L. E. B.). Upon opening the abdomen, a large spleen was visualized, adherent on all its surfaces to diaphragm, stomach, and pancreas. The spleen was freed from its nu-

Gross—(See Figure 2.) The specimen shown here consists of a spleen which weighs 1,250 grams and measures 20 by 14 by 9.5 cm. The capsule in general is slightly roughened by scattered, shredded thin adhesions and on the lateral surface shows two dime-sized areas of thickening of the zucker-guss type. The consistency is moderately firm and rubbery. The cut surfaces of the organ reveal a thin capsule and a smooth, firm, beefy red pulp with indistinguishable malpighian corpuscles. All the cut surfaces are irregularly and relatively



Graph 2

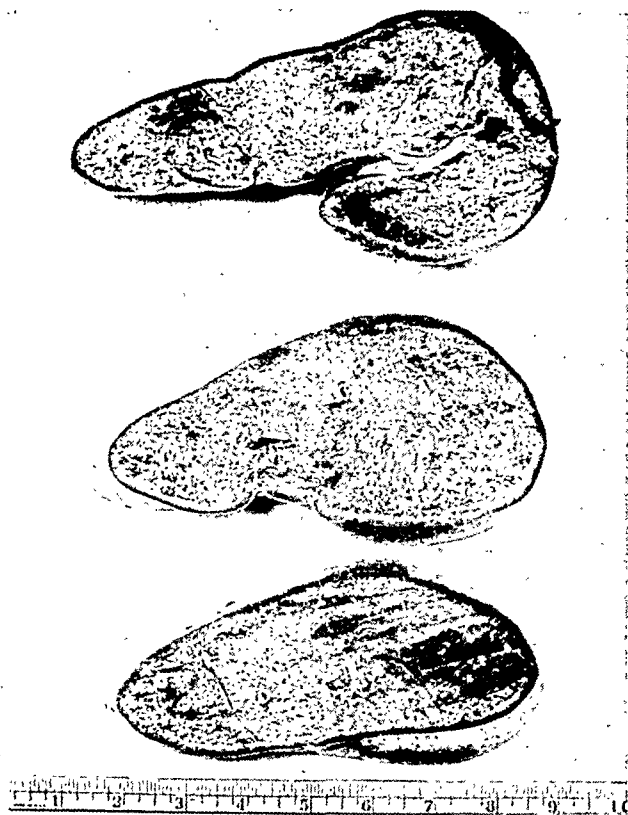


Figure 2. Cross section of spleen showing cut surfaces with thin capsule, smooth beefy red pulp, and areas of fibrosis.

sparsely stippled by tiny purplish-black areas, in the center of which there are often siderotic nodules—an opaque brownish yellow material of rather tough consistency. These combined areas rarely exceed 2 mm. in diameter. The larger vessels are not grossly remarkable.

Microscopic—(See Figure 3.) Sections examined reveal a generalized subcapsular fibrosis with hemorrhage, although the capsule and trabeculae are not notably thickened. Numerical and dimensional decrease of the malpighian corpuscles is prominent, as are periarterial and perifollicular hemorrhages, both old and recent. The sinusoids are narrow and their walls are thick and “rigid.” Phagocytosis is not unusually conspicuous.

DISCUSSION

This case is presented because of several unusual features. First, tremendous splenomegaly with the

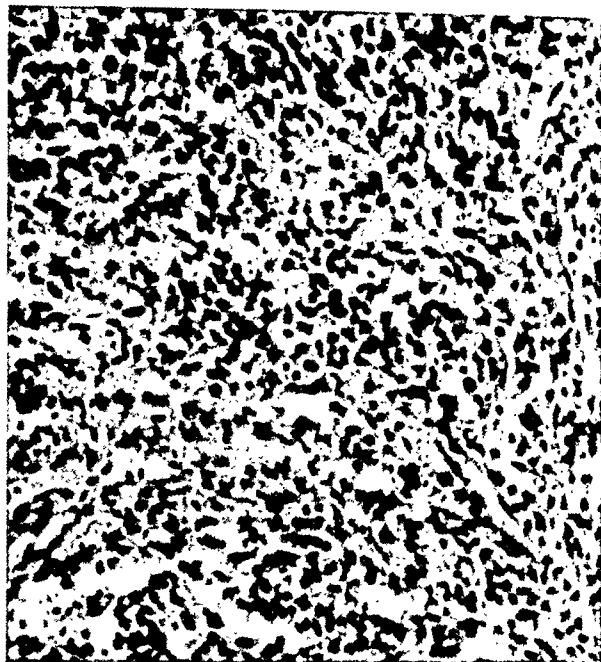
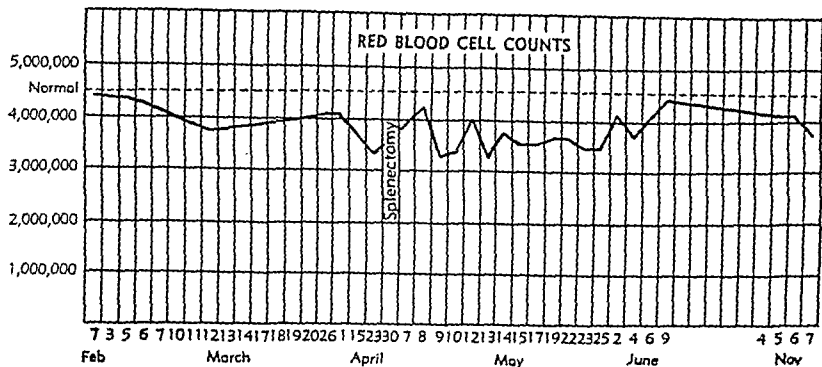


Figure 3. High powered microscopic section showing sinusoids thickened and rigid.

depression of two of the formed elements of the blood. It has been shown that anatomic enlargement of the spleen may be accompanied by depression of all the formed elements of the blood singly or collectively. Normally, the spleen is an organ in which blood cell formation, blood cell sequestration, and blood cell destruction are balanced physiologic functions. Any disturbance of this balance may lead to a variety of clinical syndromes. These disturbances may be primary (congenital) or secondary (acquired). For functional and pathologic consideration, the spleen, according to Doan and Starr Wright¹ is divided into (1) vascular system, (2) lymphoid system, and (3) reticulo-endothelial system.

When there is hyperplasia of the highly phagocytic cells, there follows destruction of red blood cells (hemolytic icterus), destruction of platelets (thrombocytopenia), and destruction of granulocytes (splenic neutropenia). These conditions are definitely relieved by splenectomy, which corrects the panhematopenia due to splenic instability.

Second, the cytopenia produced no untoward hemorrhagic effects. Symptoms which prompted



Graph 3

medical attention were those due to mechanical pressure by the spleen on the abdominal viscera. Third, following splenectomy, there was marked improvement in the subjective symptoms and laboratory findings. (See Graphs 1, 2, and 3.)

THE cause of this patient's splenomegaly is not clear. As early as 1904, Dock and Warthin² believed that the histologic changes in spleens of "Banti's syndrome" could be explained by prolonged passive congestion. These histologic changes were similar to those found in the case we are presenting. Larrabee³ in 1934, after a study of 47 cases, felt that the condition was dependent upon various intra-abdominal lesions which produced obstruction to outflow of blood from the spleen.

In 1933, Turley⁴ demonstrated that phagocytosis of perhaps extracellular enzymatic destruction of polys occurs in the spleen. He suggested that one of the functions of the spleen was disposal of polymorphonuclear cells in a normal individual. It was not until 1939 that Wiseman and Doan⁵ suggested that neutropenia was due to increased phagocytosis of neutrophils by splenic clasmato-cytes. In several cases under study by these authors such manifestations as thrombocytopenia and hemolytic anemia were present, and they sug-

gested that the spleen had undergone a change in activity so that not only formed elements which had outlived their life span were destroyed, but also mature functional elements were destroyed.

Whipple⁶ and his associates have found that the relatively great increase in splenic vein pressure in cases presenting "Banti's syndrome," when compared with venous pressures taken simultaneously on the arm, suggest that portal hypertension may be an important factor in the production of chronic splenomegaly. It is Whipple's conception that the so-called "Banti syndrome" is the result of mechanical obstruction to the flow of blood within the portal system which leads to increased portal pressure causing an engorgement of the spleen with subsequent splenomegaly. The obstructive lesion in the portal bed may be intrahepatic (cirrhosis) or extrahepatic (traumatic or inflammatory scarring and stenosis of the portal veins, cavernoma of the portal vein, stenosis of the splenic vein).

The diagnosis of the site of portal block may be suggested by several liver function tests such as high bromsulfalein retention, positive hippuric acid test, reversal of A/G ratio, and cephalin flocculation test positive. These findings would indicate intrahepatic block. If the above-mentioned tests were negative, we could assume that an extra-

hepatic block was present. Using the above criteria as a basis, it is then reasonable to assume that the patient we presented had extrahepatic block.

Whipple states that the site of portal obstruction is difficult to locate, even at operation, and that the site of portal bed block was not demonstrable in over 50 per cent of cases at the time of splenectomy at the Spleen Clinic at Presbyterian Hospital in New York. At recent operations done at the Spleen Clinic, diodrast venograms made at the time of determination of portal vein pressures, with roentgenograms at the operating table, have located the site of obstruction more frequently.

Splenectomy in the case we presented may have been curative. If the site of obstruction in the portal system was in the splenic vein, permanent

cure will result. If the block was in the portal vein, relief will have been provided for a variable period of time because of the removal of a large area of the portal bed and the interval required for portal hypertension to be built up again.

The patient returned for study six months post-operatively. Hematologic studies showed the cytopenic improvement following splenectomy was sustained six months later. Studies of liver function showed very little change from previous studies done following splenectomy. Clinically, the patient is well and symptom-free. Thus far, the benefits achieved by splenectomy have continued for a period of six months and it is felt that in this case splenectomy was warranted and of definite therapeutic value.

REFERENCES

- DOAN, C. A., and WRIGHT, C. S.: Primary congenital and secondary acquired splenic panhematopenia. *Blood* 1:10-26 (January) 1936.
- DOCK, G., and WARTHIN, A. S.: *Am. J. M. Sc.* 127:24, 1904.
- LARRABEE, R. C.: Chronic congestive splenomegaly and its relation to Banti's disease. *Am. J. M. Sc.* 188:754, 1934.
- TURLEY, L. A.: A study of the spleen in various diseases by new methods; preliminary report. *South. M. J.* 26:863, 869, 1933.
- WISEMAN, B. K., and DOAN, C. A.: A newly recognized granulopenic syndrome caused by excessive leucolyses and successfully treated by splenectomy. *J. Clin. Investigation* 18: 473, 1939.
- WHIPPLE, A. O.: Problem of portal hypertension in relation to hepatosplenopathies. *Ann. Surg.* 122:449-473 (October) 1945.

GENERAL PRACTICE RESIDENCY SET FOR NAVAL HOSPITALS

RECOGNIZING the great need for the general practitioner in the field of medicine, the Professional Division of the Bureau of Medicine and Surgery of the U.S. Navy has inaugurated a new residency in general practice in Naval hospitals.

The program, as announced by Rear Admiral Clifford A. Swanson, MC, USN, Surgeon General and Chief of the Bureau of Medicine and Surgery, will cover a period of three years and will include that phase of medicine which is required to augment the several medical specialties recognized by the American Specialty Boards. The course has been designed to supplement the residency training program, now in effect, which is designed toward supervision of physicians.

During each year of the residency medical officers will receive six months of general medicine and related specialties, and six months in general surgery and related specialties.

Staffs of the Naval hospitals and outstanding civilian visiting staffs will serve as instructors for the training program.

SCIENTIFIC EXHIBIT

The Two-Hour Test for the Early Diagnosis of Pregnancy

HERBERT KUPPERMAN, Ph. D., M. D. and ROBERT B. GREENBLATT, M. D.

NEW YORK UNIVERSITY COLLEGE OF MEDICINE, NEW YORK CITY, NEWARK CLINICAL GROUP, NEWARK,
AND UNIVERSITY OF GEORGIA SCHOOL OF MEDICINE, AUGUSTA.

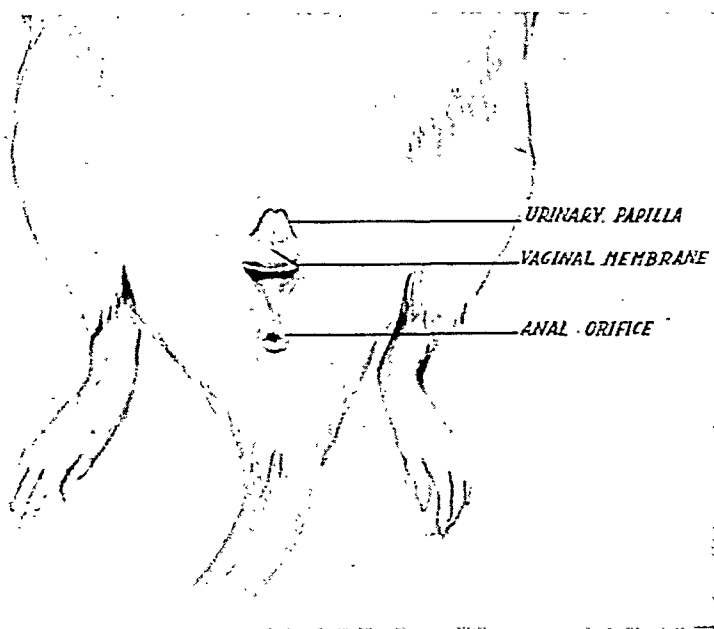
FOLLOWING the advent of the classical A-Z pregnancy test, numerous attempts have been made to shorten the original procedure. The method utilizing the action of pregnancy urine in producing ovarian hyperemia, first described by Ebersson and Silverberg in 1931, yielded the most rapid results. The evolution of tests dependent on this diagnostic endpoint is depicted below.

EVOLUTION OF THE TWO-HOUR PREGNANCY TEST EMPLOYING OVARIAN
HYPEREMIA AS ITS DIAGNOSTIC ENDPOINT

Author	Year	Time Required for Completion of Test
Aschheim-Zondek	1928	96 hours
Ebersson-Silverberg	1931	36 hours
Reiprich	1933	30 hours
Walker-Walker	1938	30 hours
Kelso	1940	24 hours
Frank-Berman	1941	24 hours
Salmon-Geist	1942	6 hours
Kupperman-Greenblatt	1943	2 hours

TECHNIC OF THE TWO-HOUR RAT PREGNANCY TEST

Selection of rats suitable for use in the two-hour pregnancy test depends on the state of the vaginal membrane. This membrane is intact in the immature animal but becomes patent when the rat attains sexual maturity. Since only immature rats are satisfactory for use in the two-hour procedure, only those animals exhibiting an intact vaginal membrane are used.

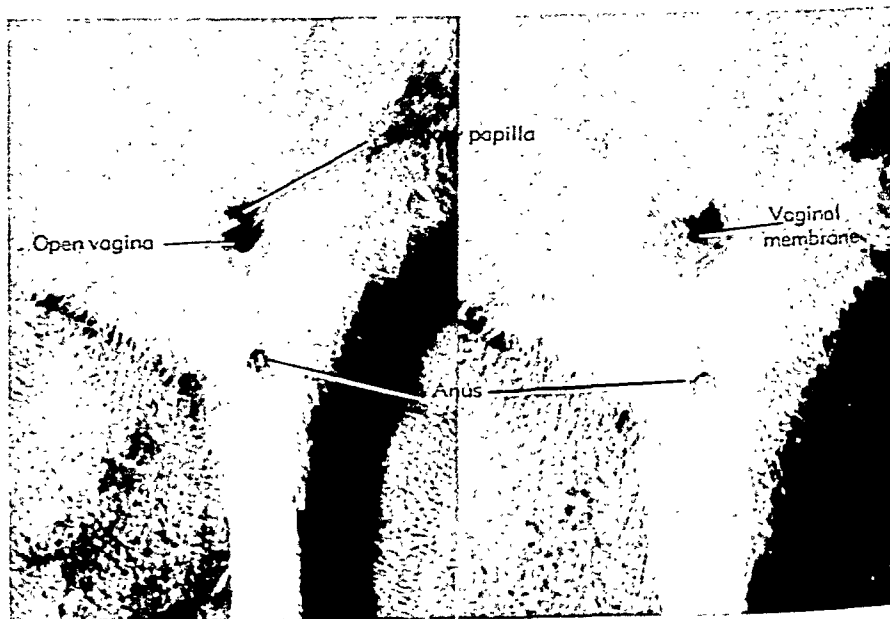


Left. Diagrammatic presentation of the external genitalia of the immature female rat.

Below. Photographs of external genitalia of the female rat.

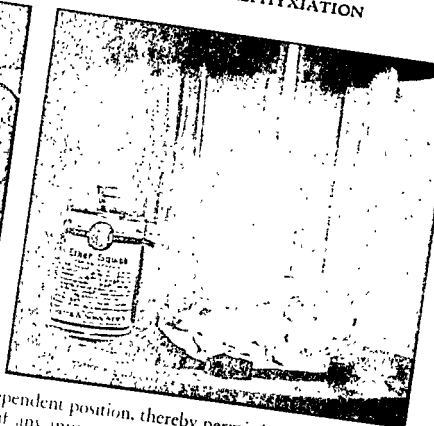
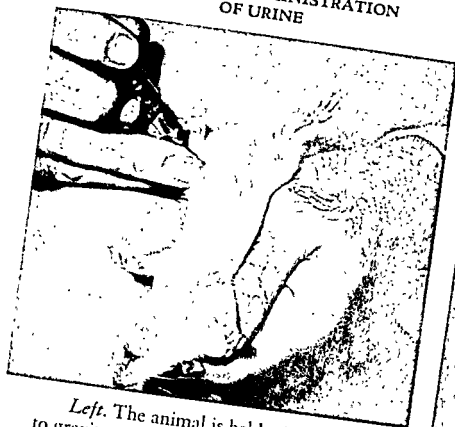
Right. Patent vagina—evidence of ovarian activity. This animal cannot be used for the two-hour test.

Extreme right. Vaginal membrane intact—evidence of sexual immaturity. This animal may be used for the two-hour pregnancy test.



METHOD OF ADMINISTRATION OF URINE

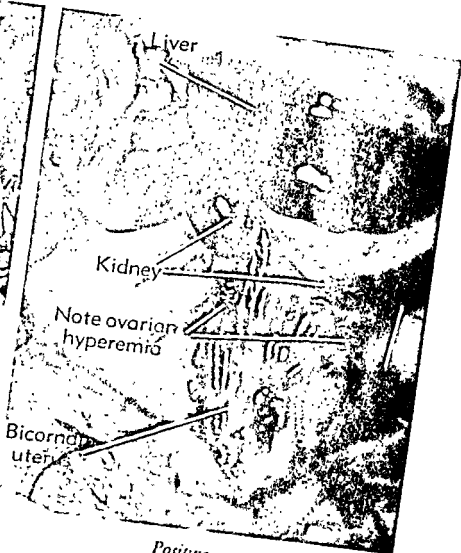
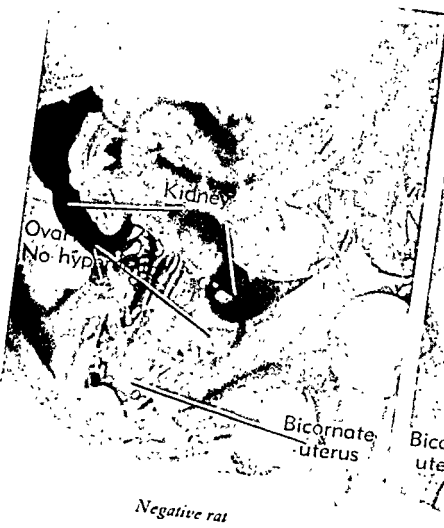
ETHER ASPHYXIATION



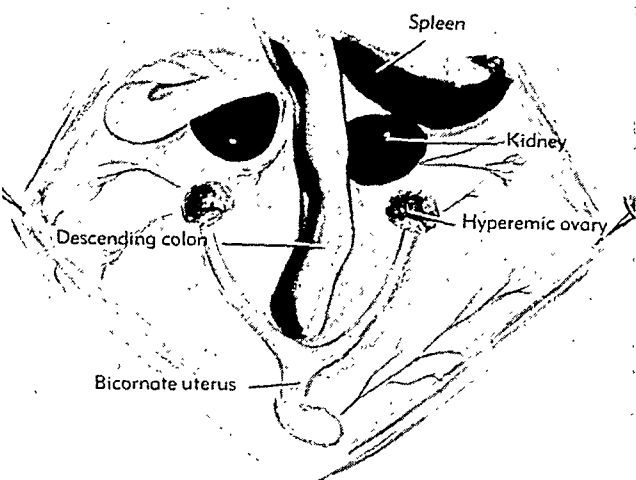
Left. The animal is held with its head in a dependent position, thereby permitting the viscera to gravitate toward the head, thus entailing little if any injury to the gastrointestinal tract by the intraperitoneal injection. One cubic centimeter of urine is injected intraperitoneally into both the right and left lower abdominal quadrants.

Right. It is important that asphyxiation be accomplished with ether since the use of other agents such as illuminating gas, etc., may predispose to false positive readings.

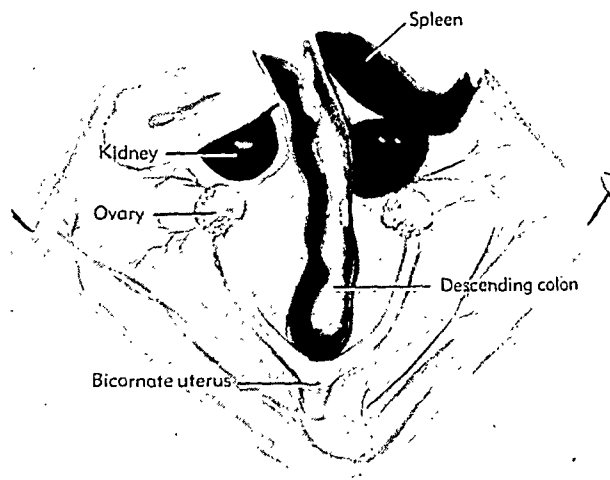
VISCERA EXPOSED



Pictorial sketch of ovaries, oviduct and uterus of negative and positive tests in rats injected with normal and pregnancy urine respectively.



Positive. Note ovarian hyperemia in contrast to lack of hyperemia of the oviduct and uterine horns.



Negative. Note oviduct and ovarian capsule are similar in color.

PRECAUTIONS TO BE NOTED IN PERFORMING THE TWO-HOUR PREGNANCY TEST

1. The animals, before examination, must be killed by ether asphyxiation.
2. In the process of exposing the ovaries, no loss of blood should result.
3. Examination of the ovaries should be made with as little trauma as possible to the surrounding tissues.
4. Ovarian hyperemia should not be read under fluorescent lighting or sunlight.
5. The hyperemic reaction is intensified if the ovaries are examined at least one to two minutes after exposure.
6. Positive reading may not be expected unless urine is examined at least one week to ten days after the missed menstrual period or twenty-one to thirty-five days after conception.

THE DIAGNOSTIC ACCURACY OF THE TWO-HOUR PREGNANCY TEST*

	Number of Tests	Errors	Per Cent Accuracy	Number of Rats
Positive	641	1	99.8	1148
Negative	636	5	99.2	1242
Total number	1277	6	99.5	2390

**Not including established cases of ectopic pregnancy*

**RESULTS OBTAINED WITH THE TWO-HOUR PREGNANCY TEST IN ESTABLISHED
AND SUSPECTED CASES OF ECTOPIC PREGNANCY**

	Number of Cases	Correct Diagnoses	Incorrect Diagnoses	Per Cent Accuracy
Established cases of ectopic pregnancy	31	26	5*	83.9
Suspected cases of ectopic pregnancy	30	30	0	100
Total	61	56	5	91.8

**Incorrect diagnosis: 3 cases necrobiosis of villi; 2 cases—few viable villi*

The two-hour test, by reason of its rapidity and accuracy, attains its prime purpose in its utilization in the detection of ectopic pregnancy. Ectopic pregnancy, an obstetrical emergency, requires rapid operative intervention as soon as the diagnosis is made. In an emergency of this type the more lengthy tests cannot be employed. The value of the two-hour test in confirming the diagnosis of ectopic pregnancy is indicated in the above chart.

**COMPARISON OF THE ACCURACY OF THE TWO-HOUR TEST WITH THAT
OF THE FRIEDMAN TEST**

	Test Employed	Number of Tests	Errors	Per Cent Accuracy
Positive readings	Two-hour test	163	0	100
	Friedman test	155	6	96.1
Negative readings	Two-hour test	155	0	100
	Friedman test	163	4	97.5
Total number tests	Two-hour test	318	0	100
	Friedman test	318	10	96.9

Five of the six false positives noted with the Friedman test were from urine specimens of menopausal patients. Since menopausal urine is rich in FSH activity, there is sufficient gonad-stimulating activity to produce ovarian stimulation and corpora lutea in the rabbit. However, FSH would not be expected to give a positive test with the two-hour procedure since LH is necessary to produce ovarian hyperemia (see chart, p. 524). Consequently menopausal urine, while capable of producing a positive reading in the rabbit, will fail to cause a false positive reaction when the two-hour procedure is employed.

GONADOTROPHIC HORMONES AND OVARIAN HYPEREMIA IN THE RAT

Extract	Dose ¹	Hyperemic Response
Follicle stimulating hormone (FSH)	1 gram 2 grams	Negative Negative
Luteinizing hormone (LH)	0.5 gram 1.0 gram	Positive Positive
Lactogenic hormone I	0.5 gram 1.0 gram	Positive (weak) Positive
Lactogenic hormone II	1.0 gram	Positive
Unfractionated gonadotrophic extract (sheep)	50 mgm. 100 mgm.	Positive Positive
Horse pituitary suspension	5 mgm.	Negative
Thyrotrophic hormone (Armour)	10 units ²	Negative
Purified pregnancy mares' serum (PMS)	0.1 mgm. 0.25 mgm.	Positive Positive
Purified pregnancy urine	3 cc. ³ 4 cc.	Positive Positive

1. Doses of pituitary preparations expressed in equivalents of dried pituitary glands
2. Rowland-Parkes' units
3. Equivalent of unconcentrated urine

The results presented on the effect of various gonadotrophic extracts in producing ovarian hyperemia show that gonadotrophins containing only luteinizing or luteotrophic activity were effective in inducing hyperemia of the ovary. Thyrotrophic and FSH preparations in the doses employed were ineffective in causing ovarian hyperemia.

ADVANTAGES OF THE TWO-HOUR TEST

1. It is the most rapid accurate biological test proposed to date.
2. Excluding cases of ectopic pregnancy an accuracy of 99.5 per cent has been attained.
3. The test animals are readily procurable and considerable variation with respect to age and weight is permitted in the choice of the animal.
4. There is no difficulty in administering the urine.
5. The actual performance of the test requires only two to three minutes of the operator's time.
6. The endpoint is easily read and requires little experience to attain a high degree of accuracy.
7. Performance of the test does not subject the patient to any discomfort or inconvenience.
8. There is no need to purify, concentrate or alter the pH of the urine prior to injection.
9. Although a morning specimen is desirable, it is not essential.

OVARIAN HYPEREMIA IN OTHER ANIMALS



Negative *Positive*
Ovarian hyperemia in the mature albino mouse.



Negative *Positive*
Ovarian hyperemia in the immature golden hamster.

THE RESULTS OF HYPEREMIC TEST IN ADULT MICE AND IMMATURE HAMSTERS*

Positive Readings				Negative Readings		
	Number of Patients	Correct Diagnoses	False Positives	Number of Patients	Correct Diagnoses	False Negatives
Adult mice	103	98	5	62	59	3
Immature hamsters	69	65	4	49	47	2

* Animals sacrificed 15 hours after intraperitoneal administration of urine

While ovarian hyperemia may be induced in immature hamsters and in adult mice by the urine of pregnant women, fifteen hours were required for the completion of the test and an overall accuracy of 95 to 98 per cent was attained. At least 3 mice or hamsters must be used for each test since a high percentage of the animals are poor reactors. Immature mice and guinea pigs were not satisfactory for use.

COMPARISON AND EVALUATION of the two-hour test with three of the procedures most commonly employed in the laboratory diagnosis of pregnancy.

TWO-HOUR RAT TEST

<i>Animal</i>	Immature female rat 21-55 days of age, 30-80 gm. in weight.
<i>Urine</i>	A total dose of 2 cc. of unconcentrated urine (morning specimen is not necessary) is injected intraperitoneally into the lower right and left abdominal quadrants.
<i>Time</i>	Two hours are required for the completion of the test.
<i>Endpoint</i>	Ovarian hyperemia.
<i>Accuracy</i>	99.5 per cent.

FRIEDMAN RABBIT TEST

<i>Animal</i>	Isolated adult female rabbit.
<i>Urine</i>	10 cc. of a morning specimen injected intravenously into marginal ear vein on each of two successive days.
<i>Time</i>	Forty-eight hours.
<i>Endpoint</i>	"Blutpunkte" (hemorrhagic follicles) or corpora lutea formation (shown in drawings next page).
<i>Accuracy</i>	97-98 per cent.

ASCHHEIM-ZONDEK TEST

<i>Animal</i>	Immature female mouse 3-4 weeks of age and 6-8 gm. in weight.
<i>Urine</i>	2 to 3 cc. of an unconcentrated morning specimen is administered in nine equal doses over a three-day period.
<i>Time</i>	Ninety-six hours.
<i>Endpoint</i>	"Blutpunkte" (hemorrhagic follicles) and corpora lutea in the ovary.
<i>Accuracy</i>	96-98 per cent.

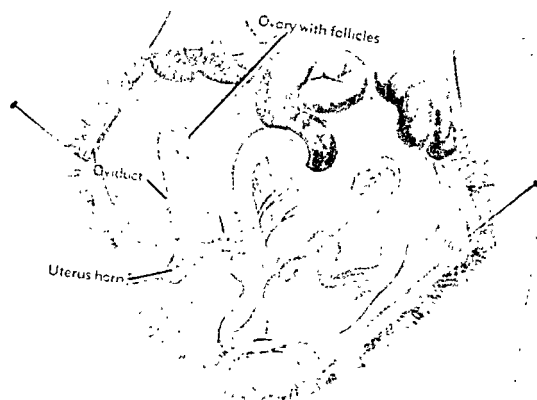
HOGBEN-FROG TEST (African Clawed Frog)

<i>Animal</i>	Adult isolated female frog.
<i>Urine</i>	80 cc. of a morning specimen are concentrated by acetone precipitation. The dried powder is taken up in 2 cc. of water. Aqueous extract is injected into the dorsal lymph space.
<i>Time</i>	Animals are observed from 6 to 12 hours.
<i>Endpoint</i>	Extrusion of eggs into water of tank.
<i>Accuracy</i>	98-99 per cent.

The accuracy of the two-hour test performed on urine samples from more than 1,200 patients exceeded that of the three procedures most commonly employed in the laboratory diagnosis of pregnancy.

The sketches below of the reproductive system of rabbits injected with normal and pregnancy urine, respectively, are presented to show differences in diagnostic endpoints between ovarian hyperemia employed in the two-hour test and corpora hemorrhagica obtained in isolated female rabbits injected with urine of pregnancy.

Negative
Note follicular development only.



Positive
Note corpora hemorrhagica.

The Medical Bookman

PSYCHIATRY IN A TROUBLED WORLD*

DR. MENNINGER dedicates his latest book to three groups: to the many millions of G.I.'s who furnished the basic facts for this study; to colleagues in psychiatry, both in and out of the Army; and, finally, to those military officers in every Division and Section of the War Department who helped toward the accomplishment of the "mission."

If anyone cares to ask, why write a book like this so long after the shooting war has ceased, the answer is that it could not possibly have been written sooner. As it now stands, some eighteen months were required to put it into print. Another reason is that psychiatry has expanded and developed as the result of war incidents to the point where it is no longer in "the rear seat in the third balcony . . . but in the front row at the show."

The first part of the book is written for the record, to set down what happened, why it happened and the conclusions to be drawn therefrom. Part II is concerned with psychiatry in peace, and hopes to be helpful to anybody who has to get on with other people; that means with the whole world in general. It is this section which will have the greatest appeal to most readers because it drives home certain facts which have evolved from the experiences of those who went to the front, and of those who remained here. The return of the soldier to his home, family, and friends was an event of the greatest importance to all concerned—not because he got back "safe and sound" in most instances, relatively speaking, but because of the inability of both combatant and noncombatant to adjust to each other. Here we have set before us the ultimate in environment and social conduct—the lov-

ing mother who has wept and worried and who loves her son better than her own life, who rushes to the swinging gate to fall upon his shoulders only to find him strange, even indifferent to her approach.

The father too finds that "Joe is different." Under Army discipline, the soldier was made to obey. He was always under somebody's watchful eye and, therefore, he became an automaton, moving this way or that like a puppet on a string, but now that he is "out," he remembers the authority of his father's restraints. They still rise up to plague him, but he is a man now, and out from under anybody's yoke—he will "show the old man where he gets off!" Personality clashes ensue with the result that parents and son are all unhappy; for "things have changed." A boy in his teens, still in high school or early college days, swung onto the last step of the disappearing train, waving merrily good-bye—off on a "lark," so naïve is youth. But the rigid training to kill his brother in war, the narrow, uncomfortable tent (without running water and toilet facilities), the anxiety for his buddies, the death and destruction always round about—all these have converted an innocent lad into a hard-hearted, devil-may-care, unemotional animal, who has become prematurely aged beyond his calendar years.

There are also the wife and child. Pictures of his baby born while the soldier was absent have been shown to every buddy or chance acquaintance with great glee, but now the child is 3 or 4 years old, refers to "that strange man," and is not easily influenced by him. There may be here more than a mere touch of jealousy and distrust. How is the veteran going to be sure that the "brat" is not from the loins of another man? The marriage, the very few nights together, the hurried departure gave no time for a blending or moulding of the young lives, and the "love" from which their sexual act sprang, may it not have been spurious and altogether untimely?

**Psychiatry in a Troubled World. Yesterday's War and Today's Challenge.* By William C. Menninger, M.D., General Secretary, The Menninger Foundation, Topeka, Kansas; Chief Consultant in Neuropsychiatry to the Surgeon General of the Army, 1943-1946. 636 pages. New York. The Macmillan Company, 1948. Price \$6.00.

And, again this matter of sex—the soldier “takes his fun where he finds it,” be he officer or the lowest in rank. Very often he cannot even be discreet about the act, and promiscuity is known and even bragged about in the barracks. It is impossible not to think that what is going on in camp may not also be going on at home. “The wife has feelings too.” The single standard maintains in books and in refined conversation, but it is not analyzed in the mind and heart of the one who is left starving for affection and companionship. It is a combination of all these circumstances which makes of War the hideous, loathsome, insane thing that it is. Men cry and have always cried Peace! Peace!! and yet there is no peace—merely an armistice, a hidden, sullen feeling of rage against the “enemy” who happens to have been born in a different locale and of a different race and creed.

All this is true and recognizable in the story of “civilization” from its first crude beginning. Man is still closely akin to the beast with all of the primeval instincts of the savage lying close beneath his social veneer. Long before the Bible was put together to be “the guide and stay” of those who seek for a better life both here and beyond, Man was doing awful things to his Brother, which were not very different from what he is doing today. And, speaking of the Bible, that great book contains some of the worst horrors in history, some of the most revolting practices recorded in the “doings” at Sodom and Gomorrah (still revolting in this day and age, and still being practiced). The Book of Leviticus, to mention only one, is replete with these vulgarities, not to use a stronger word. All of these facts, however, do not condemn nor destroy the influence of the Bible as a great book, but we can weed out the undesirable elements just as we do when reading some of the present-day pornographic novels, many of which are “well written” and manage to carry a message of good in the long run.

BUT to return to Dr. Menninger's book. Chapter 28 records the “defects revealed in civilian medicine” which have been carried over into Army regimentation, and in the passing have been magnified and no doubt worsened. There is a lack of integration; a separation of civilian from military medicine to the hurt of both. Regular Army men “kicked around” the individual doctors who came from positions of great independ-

ence in thought, word and deed to “under-the-thumb” orders of the “line organization men,” many of whom had had no medical training whatever. There were (as always) an enormous number of individuals who *knew how to win the war*, and insisted on making everybody else conform. When and where they had authority to impose their will, the going was pretty “rough” for the highly-educated, gentlemanly man of medicine. Specialists were not always regarded with favor by the Regulars; therefore, they were sometimes kept idle for months in the very presence of an urgent need for “more doctors” in the right places. Remedial or curative medicine is the *summum bonum* of every well-trained civilian doctor, but he often found himself doing “paper work” in screening, planning and administration.

As for psychiatrists, they were swamped by thousands of referred recruits who could have been helped to adjustment by general practitioners. In civilian life these G.P.'s manage to advise men and women of all stations in life, and help them over the hurdles which are quite often not too high for ordinary intelligence to negotiate. However, the medical schools seem not to have done their job in teaching even the elements of psychiatry; for the “physical” of no patient is entirely complete without a satisfactory survey of his physical make-up. Lack of recognition of this principle may account for the enormous talk about psychosomatic medicine so much in the medical literature these days. It is by no means a new thing. Our grandfathers had it, and perhaps even in greater measure, though crude, than we have had in so-called “modern medicine.”

Chapter 35 of some 10 pages is devoted to Research in Psychiatry. There is a crying need for well-trained psychiatrists who must take up the burden of the stress and strains of postwar hysteria and environmental uncertainty. It seems that in spite of all our great strides in technology, economic studies, research in physics and chemistry, and the social sciences, we do not yet know how to live happily on this mundane sphere. Unless we do learn, we shall probably go on from good to worse, from a deep and appreciative consideration of the humanities to “murder as a fine art” which takes up so much valuable time and space in the movies and on the air. Dr. Menninger's book, if carefully followed, can do much to set us right.

MEN OF MEDICINE

Scientist, Philosopher, Humanist

This biographical sketch of Dr. Myerson was scheduled for publication before his final illness. He was, however, already quite ill when he graciously consented to interviews with *Postgraduate Medicine's* staff writer. Shortly afterward, and before the article was completed, Dr. Myerson died in September of this year. *Postgraduate Medicine* is pleased to offer this article not only as a tribute to his outstanding career, but also as an impression of Dr. Myerson in what proved to be his last weeks of life.

IT MAY be a matter for controversy whether or not we are indeed a generation of vipers, but there can be little argument that we are a glib and garrulous generation. We can qualify, rationalize, evade as ingeniously and as futilely as any medieval theologian, but we shy away from anything that rings with forthrightness. Seldom do we trust words or concepts that have at their core, in spite of the abuse and accretions of time, an undimmed lustre. Such are the simple words *great* and *good*. Yet Doctor Abraham Myerson, both as man and as physician, truly merited them both.

Undoubtedly his humility and his skepticism would have made him smilingly reject the tribute, but a man's life speaks more forcefully than a disclaiming phrase—a truism that Dr. Myerson could not disavow, for he said of himself, "I am a skeptic in many of my *beliefs*, but not in my ways of life. For I believe that willy-nilly man will continue to live on this earth; that somehow I am bound to my fellows so that I wish them well and must work for and with them."

Late in the summer of 1948, those long years of strenuous work with his fellow men had etched their story in Dr. Myerson's drawn, sharpened features, in the emaciation of his always slight frame. But the deep set, searching eyes still burned with fervor as his mind pursued its lifelong quest of the answers to those imponderables: What is Man? And how is Man to achieve wisdom?

Throughout his maturity he had studied those problems, and in September of this year he died, unsatisfied with the answers he had been able to formulate. Nevertheless during the last year of his life, often bedridden and in pain, he was working on a book by means of which he wanted to share with others some of his conclusions about what constitutes the worthwhile life. Fragmentary and unfinished though it be, that volume is a source of comfort and a friendly guide toward further thought for all who may read it. He claimed little for it, referred to it lightly as a "book of degres-

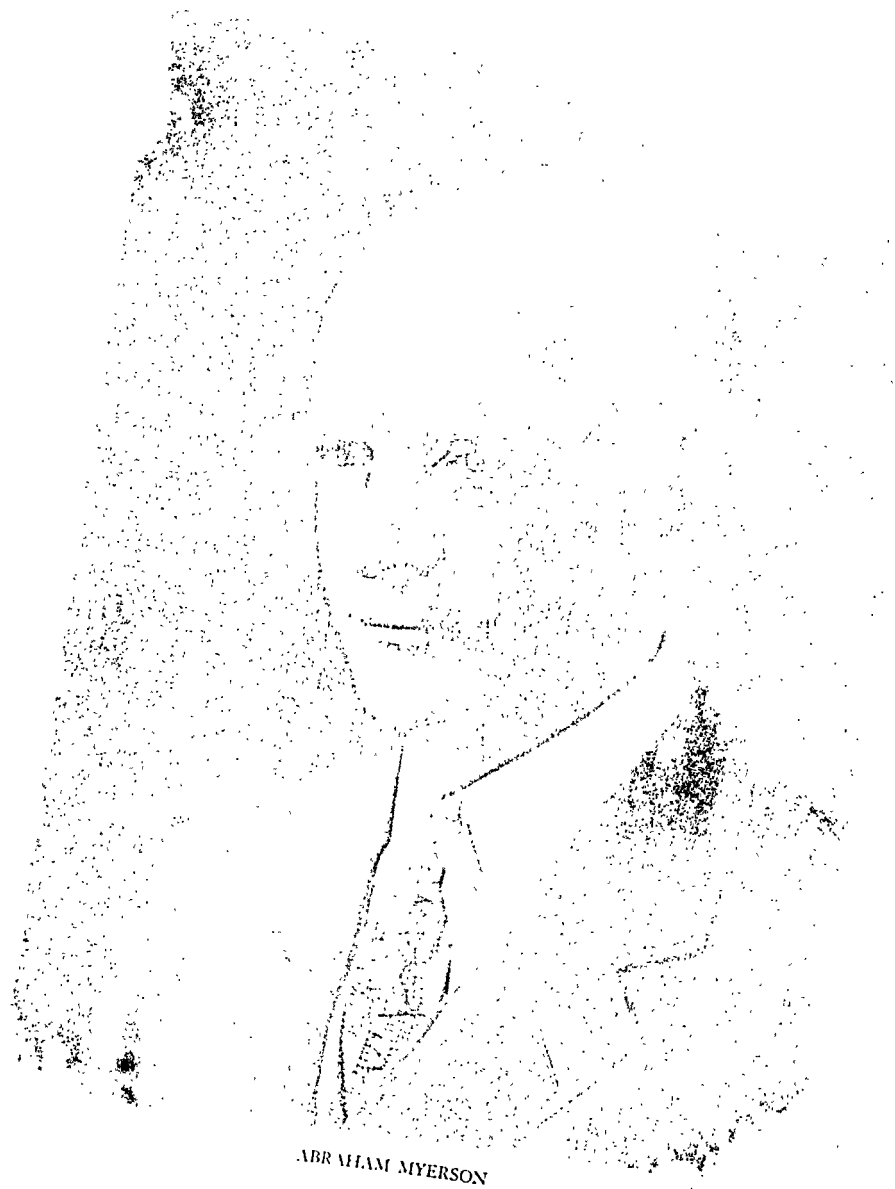
sions," but in it with deep sincerity he has distilled those convictions, founded on experience and knowledge, subtly colored by temperament, that made his life so significant.

It is not to be wondered at that a neuropsychiatrist should produce such a book, nor that all his years should have been preoccupied with the question of the nature of man. What better approach is there to that enigma than that of the trained scientist who has worked for more than two score years with that "blood-soaked sponge," the human brain? To that brain, which is man's main instrument of knowledge, come a few sensory avenues by which he can learn about the world. But let Dr. Myerson's own words speak for him.

I have dealt with that blood-soaked sponge, man's brain, for forty years as a professional neuropsychiatrist, and I have tested its functions during life and studied it after death chemically, microscopically, and diversely. I marvel at it and respect it, but it is a very limited, although marvelous, instrument at best. Even with all the tools it has created, it lives in an insignificant fragment of the universe and is subject to all kinds of diseases and disasters.

Indeed, it puzzles me why men, philosophers and some scientists talk of the MIND of Man in capitals, and as if it were too lofty to have any direct dependence upon the structure of the brain. These people seem never to have met an Idiot with no more general ideas than a puppy and, indeed, not so intelligent. Apparently they never have witnessed the decadence into imbecility of talented men via old age and cerebral arterial disease; and they never seem to understand that when alcohol changes a man from Philip sober to Philip drunk, chemistry and mind and brain have become knit as finely together as any chain of cause and effect in this world of ours.

Between the lines of this statement and permeating it throughout, is Dr. Myerson's staunch belief in the physical basis of mental disease. His approach to the nervous system and its ills was by way of chemistry, physiochemistry, genetics, and biology, rather than by way of Freud's neatly compartmentalized Id, Ego, Super Ego, etc.



ABRAHAM MYERSON

He made his opinion of the present status of psychiatry clear, and added his prediction for its future when he wrote in 1947:

The present status of psychiatry, so far as much of its work and certainly most of its publicity is concerned, is deplorable in extreme measure. The loose kind of thinking that characterizes psychoanalysis is now dominant in the public eye, but I assure you that the solid work of psychiatric research still goes on and is not greatly influenced by the hulaballoo of psychosomatics, etc. . . .

If I were asked to predict the status of psychiatry twenty-five years from now, I would state without hesitation that biochemistry, biophysics, pharmacological therapeutics will hold the center of the stage; that psychoanalysis will be present as a term, but entirely different as a system of beliefs and principles; and that the social phases of psychiatry with its genetic and social relationships will be of fundamental importance.

In all fairness to his Freudian-derived opponents, Dr. Myerson was quick to admit that he was certainly a combative person and perhaps a very prejudiced one. Certainly, they would so regard him. He was, however, not merely a theorist but a generous and open-minded person who could say in the humility that accompanies only deep wisdom that he was never estranged from his colleagues by differing beliefs, nor were his personal relationships of affection and esteem for them ever altered. "For," he mused, "in this vast and overpowering universe that surrounds us, crowds in upon us, weighs us down and inevitably molds us, how can any man have but a flicker of knowledge, an infinitesimal bit that he gratefully adds to the common store. Why should I assume that a portion of final truth has been made manifest to me alone?"

As a scientist Abraham Myerson believed profoundly in the power of heredity; as a man he demonstrated it. His father was an immigrant to the United States from a small town in Lithuania which he was forced to leave because his brother had busied himself with collecting a library for the Jewish community, and had been promptly exiled to Siberia for his effrontery. Once in this country, with a growing family to support, the elder Myerson wandered about as a peddler, then established a small and not particularly profitable business in Connecticut. Afterward he removed himself and his family to Boston where

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The three boys learned to be cocky and effective fighters—they had to be, to protect themselves against the South Boston gangs. But at home the influence of the idealistic, scholarly father was great; congeniality and companionship flourished. "By the time I was fourteen, there was no longer any conflict between my father and me. We saw eye to eye and debated endlessly matters of philosophy and history. But the odd thing was that I didn't realize there was a chance for me to become a professional man, to make something of myself until through helping my brother Joseph in some business venture, I became acquainted with some poor but very able young intellectuals in the West End of Boston. Then, suddenly, ambition spurred me to become a scientist. Why not? My older brother, after selling newspapers at twenty-two, had become a doctor. And wanting to be a free agent, hang out my shingle, and sink or swim by virtue of my own ability, I chose medicine, too.

"Of course, it wasn't as simple as that. I kept running out of money. I had to leave Columbia and come back home to Boston. I worked as a streetcar conductor. Then I managed a year at Tufts Medical School. More money troubles, and another year at Columbia. Then at Tufts I found a friend, Morton Prince, the eminent neuropsychiatrist. I was good at brain anatomy and I liked it. Morton Prince encouraged me. . . . Much later I held the chair of neurology that Prince had had."

And the amalgam of Jewish scholar and Boston's intellectual atmosphere produced a man both wise and great. Just how they were combined in one individual may best be made clear by a Jewish folk tale or fable, of which Dr. Myerson said: "This was my father's favorite story."

There once took place a conclave of scholars, and they discovered that no one had ever defined what a scholar—the word and the man—really was; so they set about making a definition. One man said this and another said that, and there was a very lively scholastic debate until an elder arose to finish the discussion.

"A scholar," he said, "is like a pin which must, as you know, have a good sharp end but, likewise, a good round end. The scholar's sharp end is to think with, his good round end is to sit down to the job with. If he has only the sharp end, he becomes a dilettante flitting from job to job, accomplishing little. If he has only the good round end, he is a pedant, unimaginative, uninspired, and learning only by rote. Yes, the scholar must have a good sharp end and a good round end."

It would be hard to find a better modern instance of the type of wise man described in that story than Dr. Abraham Myerson himself.

Perhaps one reason that he felt himself so much in harmony with Boston was that like so many of the great sons of that city, he burned with a crusading fire to help people, to make them better. But never did that zeal deny the claims of the flesh, nor labor at twisting human beings into patterns they could not maintain. Instead he worked with his patients to help them live more happily within the framework of their own limitations and handicaps whether mental, nervous, or functional.

No one who ever saw Dr. Myerson with his patients, whether in the wards of Boston Psychopathic Hospital or in the quiet restfulness of his office overlooking the Charles River Basin, could fail to be impressed by his tolerance, insight, and sympathy. Because he accepted the biological facts of life, he could help others to recognize them and to cease a futile and disintegrating rebellion.

"You see," Dr. Myerson was wont to say, "we have to deal with what people *are*—not merely with what they *do*, or even what they *become*. Heredity is tremendously important—probably the most important subject in the whole field. And there's no sense in always asking whether it's more or less important than environment. We contrast the two factors for convenience in speaking but actually we shouldn't make a dichotomy where none exists. We're too inclined to talk as though the two elements are diametrically, unalterably opposed, when as a matter of fact they're just different facets of the same thing. . . . You can't classify people in a card index, or divide personality into noncommunicating compartments as did Freud. Life and living people just aren't like that."

And Dr. Myerson, even in the last grim days of his own pain and illness, was never one to forget what living people are like.

"Next to heredity," he mused, "probably my greatest interest has lain in the search for humane drugs that will affect the autonomic nervous system. Drugs to lighten the mood, lift it from black depression to normalcy. For years we've carried on research and experiments at the Boston State Hospital—we did a great deal of the early work with benzedrine sulphate there. And in my laboratory too; many a time I've been the guinea pig myself—and aside from making the patient happier, we must find a drug to give him sleep, restful sleep, not narcosis.

"All the tension and conflicts of our life today are in a conspiracy to destroy the normal mood, to banish sleep and rest. . . . Perhaps physiologically, sleep is an anemia of the brain, an autointoxication caused by fatigue. We do know that it is the way the organism remmarshals its energies for activity. Like the appetite for food, it is caused by a breaking down of the tissues, and very likely this breaking down is to a large extent in the organs of special sense—vision, hearing, feeling, etc.

"Consciousness is essentially a product of the activities of the special senses. Yet for recuperation we must sleep. Without sleep, the burden of consciousness weighs too heavily upon us. Sleep helps all our conflicts; without it there is no enjoyment of life; fatigue kills everything, makes us incapable of realizing any satisfaction in life. Such a life is intolerable, but sleep keeps away anhedonia and gives us respite from the intensity of modern life. Very early in nearly all psychological illnesses the sleep mechanism goes wrong, and then fatigue poisons life and makes it bleak and bitter."

Dr. Myerson's last illness was complicated by sleeplessness, and the fact that his system rejected sleep-inducing drugs as toxic. His suffering shadowed his eyes and vibrated in the tones of compassion in his still eager voice.

"And then there are the popular books on psychology—usually fallacious in their optimism and their certainty of knowledge, whether that certainty be expressed or merely implied on every page. You should remember that in all science, and especially in medicine, the optimists write by far the most because pessimism doesn't pay dividends or royalty checks. Thus, if you'll just learn from me 'how to relax' says one man, you'll be all right mentally, which is like saying that if you gargle your throat, you will cure sore throat, pneumonia, and cancer. Besides, in most mental illnesses, the real trouble is that the relaxing capacity is as much impaired as the integrity of a bone is destroyed by fracture. . . ."

HE distrusted all authoritarianism, whether it was the garbled panacea of the popularizer or the pronouncement of the traditionalist vested with the weight of religion. Some of his most telling blasts against such gentry steamed forth from his reviews of psychological and pseudo-scientific best-sellers. Flanders Dunbar's book *Psychosomatic*

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or paint you a picture, or decorate your house, or entertain your friends." She is, indeed, a talented artist and painter whose gracious spirit and unerring taste are reflected in the dignified and spacious home in Brookline where the Myerson family life centered.

Anne has been studying social work at Simmons College where her father used to lecture on the psychiatric phases of social work; David, resident at Boston Psychopathic Hospital, is specializing in psychiatry; Paul, the eldest son, is a practicing psychiatrist and psychoanalyst. That last word might well have been anathema to the anti-Freudian Dr. Myerson Senior, but so broad and tolerant was the understanding between the father and son that no conflict or bitterness ever arose; the two doctors shared not only the pleasant suite of offices on Bay State Road, but in recent months the responsibility for patients besides.

"Of course, during the peak ten years or so of my practice, I saw probably 1,500 patients a year. Naturally many of them were in clinics, in state and city hospitals. And a psychoanalyst treats rather less than a dozen patients a year. Society isn't going to be healed very fast at that rate."

Its strictly limited social usefulness was but one of Dr. Abraham Myerson's criticisms of the psychoanalytic technic. More fundamental was his charge that there are no authenticated cases of the cure of serious mental illness by psychoanalysis alone. He admitted its usefulness in helping those who felt themselves bound in by their own limitations of character; such people could perhaps become better sculptors, housewives, columnists. They could, that is, if they had two or three years and several thousand dollars to devote to the adjustment of their personalities. But he was extremely skeptical of any claims that fully developed cases of paranoia, manic depressive states or severe anxiety and obsession states could be cured.

Judicious and modest in pressing his own view, Dr. Myerson ruminated on the question: "Just recently there's been one man—John Nathaniel Rosen—who claims to have cured an authentic case of schizophrenia by psychoanalysis—I won't say it's impossible."

Actually this stand on psychoanalysis was but one easily publicized strand of his fundamental disagreement with Freud and his theories. Dr. Myerson, philosopher by temperament and inclination, scientist by conviction and training, recognized Freud as a genius (a term he carefully

withheld from most of Freud's followers and interpreters) and an artist, but not as a scientist. In a criticism of Freud's theory of sex, he wrote:

Like an artist, he transforms diversity into unity by suppressing those manifestations of reality which are to him irrelevant and he boldly passes beyond proof, labeling as certainty what is merely opinion.

Like a propagandist fighting fiercely against sham and insincerity in sexual matters, he cites the positive instances only, that is those facts and cases which suit his purpose. The numberless cases which might refute his theories receive scant or contemptuous mention, while his attitude toward opponents is not at all that of a man of science, but distinctly that of the leader of a cult.

Like a mystic, to Freud everything becomes symbolic of something hidden, and nothing is what it seems to be. But the symbolism is naïve since all things somewhat straight symbolize one sexual organ, and all things somewhat round symbolize another.

POINT by point Dr. Myerson went on to refute the Freudian theories of sexual perversion, infantile sexuality, of the Oedipus complex or incest motive, and finally the analysis of dreams by the free association method. Where there is so much danger of misinterpretation, it seems fairer to let Dr. Myerson state his position in his own words.

It is impossible to discuss the validity of the free association method by which the dream shows the Oedipus complex, the father fixation, that fantasy about the mother with all the tangled skeins of lustful love and murderous hate, resistance, and the stock in trade of psychoanalyses.

Critic really one must state there is no free association method; the psychoanalyst conditions most of the responses he gets, selecting those which suit his preconceived ideas. Moreover, you can get any complex you are after just as well by ten words selected at random from a time table, as by the episodes of the dream itself. This is not an idle statement; for I have done it. It is pertinent to remark that in the first few years of my neurological experience, I sought diligently to become a Freudian, so I am not talking as one who has always been a skeptic.

There speaks the scientist whose common sense endeared him to many and commanded the respect even of those who disagreed. Too often the cloak of plain speaking is boorishness, but Dr. Myerson is meticulous in judgment and graceful in praise.

It may seem presumptuous for anyone but a Havelock Ellis to criticize Freud since these are the two names most



DR. MYERSON IN HIS LABORATORY

associated with the study of sex in our times. Yet the technic of science is something which even the humblest may understand, and anyone whose daily work brings him the same contacts as those through which Freud himself has established his doctrines may properly criticize both the technic and conclusions of this great man.

History records many eminent men who have been as eminently wrong. The genius of Freud resides more in his influence on mankind than in his direct work. Right or wrong as his conclusions may be, or as time will judge them, he has forced us all to dig more critically, explore more candidly into human morals and human conduct. He has helped break down sham by tearing away its cloak, shame. He has made what we foolishly call obscenity a matter which we may study as objectively as in botany we study the stink weed and the rose. He has contributed to the result that all the phases of sexuality are losing their aboriginal powers to cripple and maim our grip on reality. Any man who has this as his achievement deserves the esteem and gratitude of all mankind, of those who reject his specific doctrines as much as those who accept them.

Dr. Myerson was quick to recognize how great is our ignorance of the origin and progress of mental illness. "The sad fact is that we're still very ignorant of much that constitutes mental health and mental disease. . . . Our field is one in which

theories reign; it is the least accessible to scientific method, largely because the mind of man offers no field for experimentation comparable, let us say, to the functions of the liver."

Dr. Myerson was ever eager to pursue the scientific method, to study facts rather than speculate on theories. At the end of his extraordinarily active and useful life, there was one accomplishment that seemed to him more important than anything else.

"It seemed theoretically correct that if one could study the blood directly before it reached the brain, and then could study it directly as it came from the brain, without admixture with venous blood from other parts of the body, something might be learned of what takes place within the brain."

It proved possible to obtain an internal carotid artery without the use of the ordinary

Luer syringe—a technique without danger, looks familiar and entirely

Used together with the technic seems a

of brain metabolism. In addition the results of disease processes within the brain may be ascertained in some measure by this combination of jugular and carotid puncture.

This contribution, reported in the *Archives of Neurology and Psychiatry*, as "Technic for Obtaining Blood from the Internal Jugular Vein and the Internal Carotid Artery," provided a new method of studying at first hand the metabolism of the brain, and was developed in collaboration with two other Boston doctors.

Estimating such a skilled but purely mechanical procedure as his greatest contribution to the field shows clearly the direction from which Dr. Myerson expected progress in the successful treatment of mental ills. That others shared his beliefs was evidenced by several of the papers presented at Washington, D.C. in May 1948 at the second annual scientific meeting of the Society of Biological Psychiatry.

Another way of indicating the same road was Dr. Myerson's use of the electric shock treatment in depressive states of old age and psychoneurosis. Incidentally, though the procedure was originated by two men in Italy, then tried in England, and introduced here by Dr. Lothar B. Kalinowsky of New York, Dr. Myerson himself did a great deal of pioneer work in the treatment, teaching it to state hospital staffs throughout New England. After seeing its beneficial results in hundreds of cases in state or city institutions, and in selected private cases, he observed that it worked exactly as successfully when given as routine treatment without saying a word to the patient, as it did when used as an adjunct to carefully controlled interviews and elaborate explanatory build-ups. Such a view held no cynicism; it was logical to expect it from the author of a study: *The Treatment of Hysterical Amnesia by Purely Pharmacologic Means*.

His colleagues in the profession, whether they agreed or not, were firm in their respect and warm in their affection for Dr. Myerson. Their respect was based partly on the fact that by instinct, training, and experience he was a very fine doctor.

"He'd listen to a catalogue of aches and pains as long as your arm, and somehow go right to the cause of the matter. He didn't wear blinders because he was practicing psychotherapy. As a diagnostician he was tops. . . . And in spite of his therapeutics, sincerely held though they were, he leaned further toward Freud in interviewing and treatment than you'd suspect from reading his pub-

lished articles. He was never one to pass out a few nembutal pills to a woman who complained of sleeplessness without asking some pretty searching questions about her sex life!"

PATIENTS, whether they came hesitantly to the dignified office on Bay State Road, or faced the slight dynamic figure in the drabness of a public institution, were quick to respond to his warmth. To him they poured out the gnawing anxieties and shamefaced fears they had long buried even from those closest to them. Dr. Myerson's personality was warm, open, forceful. He had a photographic memory and an enviable ability to pierce through the tortuous superficialities to the very seat of the trouble. He had confidence in his patients, inspired sometimes in them.

Sometimes the situation demanded ingenuity as well as confidence. There was, for example, the case of the female patient who, typically in love with her psychiatrist, craftily locked herself in the bathroom of the office suite overnight so that she could seduce the doctor the next morning. All attempts to get her out were futile; her well-known name forbade forcible ejection by the Boston fire department. The doctor arrived; he smiled thoughtfully, and tapped gently on the door. Silence within while he murmured softly through the panel. Promptly the door was unlocked, the patient eagerly came out, and happily went down to the automobile waiting to take her to the Boston State Hospital.

"But Dr. Myerson, what on earth did you say to her?"

The doctor's wise smile deepened; his clear eyes twinkled. "I just asked her how she could possibly consider eloping without shopping for a trousseau first."

The adjustment of the individual to society was a problem that claimed his attention early and that never ceased to interest him. To him it was not merely a question of how this harmonious adjustment could be brought about, but whether it ought to be done at all—the whole question of the advisability of fitting man, basically an animal creature of instinctual drives and urges, into a complicated framework of forces that reach backwards to the earliest days of the race. "The dead hand rules,—yes, and the dead thought, belief, and custom continue to shape the lives and character of the living. The invention and development of

speech and writing have brought into every man's career the mental life and character of all his own ancestors and the ancestors of every other man."

THIS cleavage between what man is and what society expects him to be never ceased to stimulate Dr. Myerson's thinking. In the last months of his life he found himself extremely depressed by it. "A society that twice within a man's lifetime can erupt into war so violent that it comes close to destroying all that men have so laboriously built up—a society that now holds in its awkward grasp the weapon with which it can annihilate itself—how can man—or man's pitifully primitive nervous system—adapt itself to living in such vast and over-reaching shadow?"

But his despondency was perhaps a symptom of his illness. Certainly his friends and colleagues like to remember the earlier years of dynamic energy and optimistic vigor. Often he would teach in the morning—he was at one time professor of neurology at Tufts College Medical School and at another clinical professor of psychiatry at Harvard—see patients in the afternoon, squeeze in a court hearing, look in at the laboratory, visit the jails, and perhaps write a chapter or two of a book in the evening. Dr. Leo Alexander, the burly and brilliant Viennese who was first his protégé, then his research assistant and associate, and who is now his successor with the resounding title, "Director of Neuro-Biologic Unit of the Division of Psychiatric Research of the Boston State Hospital"—Dr. Alexander affectionately called him *The Happy Warrior vs. Fads and Fancies in Psychiatry*. That title is a tribute to his solid common sense; his wit and sharp lucidity were equally memorable. Dr. Myerson had "experted" at murder trials in Boston for many years. Whenever he was present the court was sure of a scientific, sensible, well-documented point of view. Experience helped him; he knew all the celebrated criminals from Sacco and Vanzetti to the traitor, Best, the malodorous radio broadcaster of World War II, who by a quirk of chance was tried in Boston instead of Washington.

Once, on being presented with that ancient conundrum, "Now tell me, in your opinion, can the defendant distinguish right from wrong?" Dr. Myerson responded thoughtfully: "Ah yes, the defendant knows right and wrong precisely as the house cat knows that it is Sunday—without fully

appreciating the sanctity of the day."

Something of the same nice balance of thought characterized his comments on Sacco and Vanzetti, the famous pair whom he knew intimately, visiting them in the Dedham jail almost every day for seven years while he was doing research for the state on criminals. During that time Dr. Myerson formed a shrewd opinion of the men and their respective characters, but he was too cautious to make an unequivocal statement on their guilt.

"Vanzetti, the fish peddler, had more brains—alert and interesting kind of chap. And guilty or not, they certainly didn't have a fair trial; now if in the first place they'd had a lawyer as good as William Thompson, their last defense counsel, the outcome might have been different. That's entirely apart from the fact that they were both avowed anarchists and certainly potential killers.

"You know people are always asking about 'the criminal type.' We no longer believe in determining such a matter by cranial characteristics, but nevertheless people don't realize what an infinitely delicate adjustment of factors determines character. There are all the X's of heredity plus the accidents of what happens to anyone. Sometimes I look at a criminal and think, 'There, but for the grace of God, go I!'

"There is though a certain predisposition in that some people have absolutely no altruism in their makeup; they recognize no human rights but their own. That's a constitutional psychopathic type.

"And another thing most of us overlook is that crime is a disease of youth. If the offender belongs to a wealthy family, he's protected, everything's hushed up, time and again perhaps, until he finally learns that crime doesn't pay. Then his anxious family sigh with relief and watch him 'settle down' into a stout householder and good citizen."

Boston held for him always, as it had for his father before him, a promise and a fulfillment that never failed them. It was a feeling difficult to put into words. For the doctor in his last days it was symbolized by the gracious home in Brookline surrounded by broad lawns drowsing in the hush of late summer. "In what other city could I enjoy all this peace and privacy only ten minutes from my office? And my children have been brought up here; they love it too—and people know me—" The doctor lifted his hand toward the flowers and dappled sunlight beyond the French doors, but his eyes searched for something he could not point out.

YEARS ago as a promising young neurologist working at Harvard, Myerson answered a call from St. Louis University for a bright young man in research and teaching. There he worked under the direction of Dr. William Washington Graves, and by his ability and promise so endeared himself to his chief that Dr. Graves invited the Boston youngster to practice with him. For his part Myerson was devoted to the big, rangy Kentuckian with his gusto and breezy enthusiasm. Moreover he admired him for the way he had turned defeat into challenge. Dr. Graves had been a surgeon, a fine surgeon, but he had also been a pioneer in testing the possible beneficial uses of x-ray. In the course of that research he became sterile, his face was disfigured, and his hands so badly burned that he could no longer operate. Undaunted, he began a new course of study in this country and Europe, emerged as an outstanding neurologist.

Just about the time that young Myerson was considering his chief's offer, Elmer Southard of Harvard also wrote, inviting him to "come back and work at the new Boston Psychopathic and be on my staff." Again the New England city exerted its fascination for him. "It wasn't just the place that pulled me back. There was a certain very charming and artistic young lady. I loved both the city and the woman—not that she wouldn't have gone anywhere with me—." The possibility of even a momentary misunderstanding of the relationship he so cherished roused the doctor from his mood of reverie.

"Dr. Graves volunteered some very good advice at that time. He knew me well enough to realize that my heart called me back to Boston, and he warned me not to be a masochist—told me flatly to follow my egotistic will and benefit myself. So back to Harvard it was. And a couple of years later I was made Clinical Director and pathologist at the State Hospital at Taunton, Massachusetts. I was there four years; my oldest boy, Paul, was born there." A wistful smile curved the doctor's pale lips. "Did you know his middle name is Graves?"

From the early days at Taunton his interest in heredity was unflagging, and while admitting our ignorance of how it works—we know only that deviations from normal start in the germ plasm—he never ceased to emphasize its importance. Toward the end of his career he was consulting psychiatrist at McLean Hospital at Waverley, Massachusetts. More than one visitor to the sanatorium's

beautifully laid out grounds and expensively equipped buildings has been struck by the fact that it shares with Harvard University lavish benefactions from some of New England's most prominent families.

Over the years of teaching, research, practice, and lecturing Dr. Myerson's influence was strongly felt, not only in his home city and state, but throughout the country and the world. This influence was exerted through his reports and studies of work done under his direction; through the active part he took in the projects of the American Psychiatric Association; through the many positions of honor and service he filled so ably. For years he was Chairman of the Committee for Research for the American Psychiatric Association, a job that had international as well as national significance. By his energy and persuasiveness, he got the Department of Mental Health to subsidize such worthwhile projects as new methods for the state hospitals. Indeed the whole Department of Mental Health Research Committee developed under his dynamic guidance from informal get-together meetings for discussion to a very important factor in the mental health of Massachusetts and the United States. The men discussed technics, outlined definite research problems, exchanged ideas, decided on a common nomenclature for the rapidly expanding field of psychoneurological science.

During the crowded years of teaching, research, writing, and private practice, Dr. Myerson held many positions of importance. For some years he was the chief medical officer at Boston Psychopathic Hospital, and throughout his career he acted as consulting neurologist for that institution. He served in that capacity also for Washington Hospital, McLean Hospital, Boston City Hospital. At Beth Israel he was long chief of neuropsychiatry; at different times he was a professor of psychiatry at Harvard, of neurology at Tufts. He was director of research for Boston State Hospital; an active member of the Committee on Research in Mental Health, Commonwealth of Massachusetts.

In 1935 the Rockefeller Foundation began its active support of his research laboratory, a working center of great value to the whole field of mental health. Several times he attended medical congresses abroad; he was a member of the American Medical Association, the American Neurological Association, the American Psychiatric Association, the American Psychopathological Association, and

the Phi Delta Epsilon fraternity. In addition, he bore the title Diplomate, American Board of Psychiatry and Neurology.

As his strength diminished he would have been glad to shift some of the burden of responsibility, but the depleted hospital staffs and increased demands of the war years found him valiantly responding. His health suffered from the strain, and by January 1947 he began to resign from as many of his posts as possible, though he continued to see patients even in the intervals between hospitalization periods and to within a month of his own death.

AND so there came to the end of his life a man who was both wise and good—an inimitable mixture of salty realistic earthiness and a probing, restless mind. All his years he had been guided by an idealism that, with warmth and humility, embraced all mankind. He had been permeated, as had his father before him, by optimism; but at the end of his journey he was filled with bitterness that man's way was so clouded, that so little had been accomplished. He had been a fighter for the truth as he saw it, yes, but the truth had not set him free. For, to be violently partisan enough to fight, to be that far emotionally off balance, means that one automatically loses his clarity of judgment. On the other hand, if one is perfectly open-minded and impartial, he is paralyzed by that objectivity and loses the impulsive force to act. He had been a liberal—yet liberals are not tough enough to survive this chaotic, disintegrating world.

So at the end, again like his father, he declared himself a pessimist. But surely that dark mood was but a reflection cast by the suffering body on the clear spirit of one who understood the human soul. Unflinchingly he had uncovered its greed, its pettiness, its self-seeking, yet never had he despised mankind nor held himself apart. He knew that all men are brothers and he served them unstintingly. Not that they erred, but that they squandered their highest potentialities filled him with sadness.

Perhaps it is more just to summarize his views by words printed some years ago in *The Caduceus*, the Tufts Medical School year book, in which he spoke seriously to the students who loved and honored him.

When one contemplates the disturbed, even chaotic world in which we at present live, it is hard to feel that there is

any essential law of progress or that mankind moves forward in a direction in which there may be both development and growth of his personal character and of a better ordered, more equitable society.

There is one field of man's activity, however, in which steady, definite progress is seen and that is *science*. Year by year man is bettering his understanding of the universe in which he lives, and is able to manipulate the forces of life in a more orderly, more useful, and at the same time, more powerful manner.

In the field of neurology and psychiatry progress seems slow and practice discouraging, if we take the short view of our work, the day-by-day outlook. But if a man takes the long view, let us say one which embraces a quarter of a century and considers what has happened in this field in that period of time, he becomes optimistic. He sees mankind, as personified by the group of men working in this field, conquering its problems, passing onward to better understanding and to better manipulation of natural forces for the purposes of prevention and cure.

There speaks the neurologist, the scientist, the disciplined but aspiring mind of a doctor great in his generation. But Dr. Abraham Myerson was also a philosopher who pondered for a lifetime the immemorial question, "What is man?"

This is how he answered.

To me Man is a thickened node in the invisible web of a universe of forces which, ever repetitively and ever anew, flows in and out of him; and he is part of an Ecology which involves plants, other animals, climate, soil, all kinds of radiant forces and chemicals. He is united by the invisible strands of Heredity to every form of life that ever lived, and his fundamental drives and compulsive activities go back to the first piece of life that ever appeared on earth.

He is immersed in age-old and ever-changing social forces which compress, enhance, destroy or deform his trends. He is beset by conflict between his biology and his sociology at every step. He is the victim and the profiteer of his cunning hands and his fatal words. Within him there rages an Inner Turmoil made up of his memories and especially words, the most important of which are I, You, We, They, and the most fatal, You, when the man learns to address *himself* by his ominous term. He is abrim with chemical factories; in fact, every cell is a better chemist and physicist than all the Nobel prize laureates put together, and somehow there is a constant and shifting balance of forces which includes hormones, ferments, enzymes, memories, ideas, emotions, moods, and all of which is an unexplainable transit from conception to that catalytic dispersal, perhaps reassemblage, called Death.

Only by remembering the range of his experience, the penetration of his knowledge, and the breadth of his compassion, can we measure what humanity has lost in Dr. Abraham Myerson's death.

LUCILE C. DEINARD



EDITORIALS



HIGH FAT DIETS AND CORONARY DISEASE

FOR some time past there has been a growing conviction on the part of many cardiologists that there is a connection between fat metabolism and intimal atherosclerosis, especially of the coronary arteries. More and more evidence, experimental and clinical, has been found to support the idea that there is a disturbance, either on the part of the body as a whole or locally within the walls of the arteries, in the metabolism of fats, especially cholesterol.

Some of the points in favor of this idea are the following: the fact that the early intimal atheroma consists almost entirely of cholesterol; the low incidence of coronary disease among certain races having diets low in fats; the increased incidence of coronary disease in persons with high blood cholesterols, whether familial or due to disease such as myxedema; the ability to produce atheromatosis in certain experimental animals by the forced feeding of cholesterol. According to Moreton, the repeated ingestion of meals high in fat may produce atheroma even though only a small percentage of the fat is in the form of cholesterol.

There are still many problems to be solved before the exact role of fat in the diet can be evaluated as far as coronary disease is concerned. It is not yet known definitely whether diets high in fat can initiate coronary atheromatosis in human beings. However, there is now some evidence that high fat diets may be harmful to those persons who already have coronary artery disease.

Although the considerable incidence of peptic ulcer in patients with coronary disease is probably coincidental, an empirical survey seems to indicate that the usual ulcer diet, rich in fats and cholesterol, tends to have an adverse effect on the course of arterial disease.

In the first group of 10 patients whose histories were reviewed, 9 were found to have peptic ulcer. All of these patients died, but their histories exhibited remarkable similarities. All the patients were male, ranging in age between 38 and 55 years, and all were known to have coronary disease. In each case, the patient died within seven months after a high fat diet was instituted. In the one case not involving a stomach ulcer, the patient was placed on a high fat diet following a severe respiratory infection.

The second group whose records were examined consisted of 17 patients who were known to have coronary disease and who developed symptoms of peptic ulcer one or more years after the diagnosis of cardiac illness was definitely established. All of these patients are living, but after they had been put on the usual Sippy regimen with its high fat content, 12 of the 17 suffered aggravated symptoms of angina pectoris within a period of one to three months after starting the ulcer diet.

It should be noted that so far we are unable to state that a diet high in fat will initiate atheroma in otherwise normal individuals. It seems highly likely, however, that the ingestion of excessive amounts of lipids may cause deterioration of an arterial wall already the site of atheroma. This is analogous with the recent finding by Paterson that in certain ani-

mals the forced feeding of cholesterol resulted in an increased incidence of arterial disease but no further damage in those animals already having intimal changes.

Although the total number of cases studied thus far is too small to justify any positive conclusions, the results were striking enough to warrant further investigation of the relationship between cholesterol metabolism and atherosclerosis and to use caution in recommending a high fat diet for patients suffering from coronary cardiac disease or persons, such as those suffering from diabetes, hypertension and myxedema, in whom there are potentialities for coronary disease. In such persons, it would seem wisest to use ulcer regimens in which frequent feedings of foods that are low in fat are emphasized.

M. P.

BACITRACIN

THE superiority of bacitracin in an ointment base over the sulfonamides, penicillin, and furacin in the local treatment of primary and secondary pyogenic infections of the skin has been reported by Drs. J. Lowry Miller and Meyer H. Slatkin and Balbina A. Johnson, A.B. The advantage found in using bacitracin was that it resulted in a lower rate of sensitization of the patient while remaining as effective as the other chemotherapeutic agents with which it was compared. Its use has been somewhat restricted by the necessity for refrigeration of the ointment to maintain its potency. Five hundred units of bacitracin per gram of ointment base was the strength employed by the New York investigators.

Comparisons of the degree of sensitivity experienced by patients treated with the different medications showed that in early use, penicillin sensitized 6 per cent of cases, the sulfonamides 5 per cent, and furacin 5 per cent, while only 0.5 per cent of patients experienced any sensitization from bacitracin.

In their report, Miller, Slatkin, and Johnson stated, "We have used bacitracin for as long as

three hundred days in the same patient without producing reaction. In infectious eczematoid dermatitis and folliculitis of the beard a contact dermatitis-like reaction from medication is prone to occur. We have encountered no such reaction with bacitracin. In fact, we used bacitracin ointment successfully on a patient with folliculitis of the beard who at the time was suffering with a dermatitis from sulfathiazole ointment."

A considerable amount of experimental work was conducted in an attempt to find an ointment base in which bacitracin remained relatively stable at room temperature, which released the bacitracin when in contact with the tissues, and which was acceptable to the patient. Oil in water and greaseless Carbowax bases were found to fulfill these conditions best. Clinical trials were made of the ointments which appeared to be effective on the basis of laboratory tests. Formulas were given for two ointment bases, in which bacitracin remained therapeutically effective for at least two weeks without refrigeration.

A. E.

"IMPROVING" AGENTS FOR THE TREATMENT OF FLOURS

THE CAUSE of so-called canine hysteria, running fits, or fright fits in dogs has been known since 1946. At that time Mellanby¹ demonstrated that the responsible factor was "agene" which is defined as 1 per cent nitrogen trichloride in air saturated with water vapor. The purpose of this substance added to flour is to alter the baking characteristics.

The first observable symptoms produced in dogs placed on a diet of agene-treated flour consist of general lethargy and muscular incoordination. With advanced stages of poisoning, the animal behaves in a panic-stricken manner, throwing itself against the side of the cage, howling piteously, and clawing the air. If the hysterical animal is let out of confinement, it will run wildly about, bumping into objects which get in the way. In the severest form of poisoning epileptiform, or tonic-clonic,

convulsions may occur which can be so severe and continuous that death ensues.

Other substances such as chlorine, nitrogen, and benzoyl peroxide treated flours do not harm dogs. Apparently the toxic principle of agene-treated flour is associated with a protein fraction, and according to a recent study by Radomski² and his colleagues the most likely toxic principle seems to be a di-, tri-, or polypeptid absorbed intact into the blood stream.

The production of fits by a diet of agene-treated flour is not peculiar to dogs; Radomski and his colleagues demonstrated the same or-

der of sensitivity in rabbits and to a lesser degree in cats. Rats and Rhesus monkeys, however, are apparently resistant to the manifest symptoms. The question of possible toxicity to human beings is still unsettled, but it scarcely seems desirable to include such a possible toxic agent in flour from which most daily bread is prepared.

1. MELLANBY, E.: Diet and canine hysteria. *Brit. M. J.* 14:885 (December) 1946.
2. RADOMSKI, J. L., ET AL.: The toxicity of flours treated with various "improving" agents. *J. Nutrition* 36:15-25 (July 10) 1948.

E. P. J.

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Medicine Makes the News

LASKER AWARDS PRESENTED FOR MEDICAL LEADERSHIP

IN RECOGNITION of their outstanding contributions in the fields of medical and scientific research, medical hygiene and public health administration, eight leaders in these fields recently received the 1948 Lasker Awards of the American Public Health Association.

Recipients of the awards for outstanding scientific research and study are: Dr. Selman A. Waksman of Rutgers University and the New Jersey Agricultural Experiment Station, and Dr. Rene J. Dubos of the Rockefeller Institute for Medical Research, New York City, jointly, for "studies of the antibiotic properties of soil micro-organisms," and to Dr. Waksman also for the discovery of streptomycin.

Dr. Vincent du Vigneaud, head of the Department of Biochemistry, Cornell University Medical College, New York, "for studies of transmethylation and contributions to the chemistry of biotin and penicillin."

For outstanding administrative achievement the Lasker Awards were given to: Dr. Martha M. Eliot, Associate Chief, U.S. Children's Bureau, Washington, D.C. "for organization and operation of the Emergency Maternity and Infant Care Program."

Dr. R. E. Dyer, Director, National Institute of Health, Bethesda, Maryland, "for organization and administration of the Research Grants Division of the National Institutes of Health of the U.S. Public Health Service."

Cited for "outstanding accomplishments in the education of the physician in the psychological aspects of the practice of medicine," was Dr. C. Anderson Aldrich, Director of the Rochester (Minnesota) Child Health Institute of the Mayo Clinic.

The Lasker Group Award this year honored: The Department of Medicine and Surgery, Veterans Administration, and especially Dr. Paul R. Hawley, its former Chief Medical Director, and Dr. Paul B. Magnuson, Chief Medical Director, "in recognition of the efficient program developed by them to provide medical care for the millions

of veterans who helped in the defense of America during World War II."

WAKSMAN AND DUBOS

"Their (Waksman and Dubos) studies on the relation of the association and antagonism of mixed microbes of the soil have demonstrated the antibiotic properties of soil bacteria to be of inestimable value to man's improved health and well-being," says the awards committee. Dr. Dubos' theory was that "in nature, all organic matter is decomposed through the agency of micro-organisms."

He experimented with the causative agent of boils, the staphylococcus, and found another agent in the soil which attacked them. Seeking to find what there was in this bacillus that killed staphylococcus, he found the answer in a fraction of the bacillus called tyrothricin. From this, he separated gramicidin, the first antibiotic used clinically in recent years. This was done and reported on in 1939.



RENE J. DUBOS



SELMAN A. WAKSMAN

After two years at Harvard Dr. Dubos returned in 1944 to the Rockefeller Institute where he is engaged in tuberculosis research. He hopes to identify that component of the TB bacillus responsible for creating the disease in man, and also the factor which causes a virulent bacillus to become nonvirulent.

The discovery of gramicidin enlivened interest in the subject of antibiotics generally. Penicillin followed,

and four years ago, Dr. Waksman and his students discovered streptomycin. The basic research that led to its development began in 1915 when Dr. Waksman graduated from the then Rutgers College and began digging holes in the New Brunswick, New Jersey, campus to isolate the soil microbes. Study of the relationships of microbes to soil conditions, decomposition, etc., laid the foundation for the discovery of several antibiotics including streptomycin.

DU VIGNEAUD



VINCENT DU VIGNEAUD

Dr. du Vigneaud is honored for "advancing the frontiers of our knowledge of fundamental living processes" in the science of biological chemistry. Out of an early interest in sulfur compounds, their structure and metabolism. Dr. du Vigneaud developed a new concept regarding the essential role of methyl groups and amino acids in the body.

These discoveries are in-

valuable to medical understanding of the functions of the liver and kidneys. "They have given many new windows," his citation points out, "through which the chemist, the biologist, and the physician can visualize changes that characterize all living cells."

Dr. du Vigneaud is rewarded also for his accomplishments, in collaboration with others, in the studies of vitamin H, or biotin, a member of the vitamin B complex. He helped prove the identity of biotin as more than a yeast growth factor, helped isolate it, and worked out its chemical structure, all since confirmed.

ELIOT

Against deaths associated with childbirth in the United States, the nation's third highest death group, Dr. Eliot for more than twenty-five years, has fought as an advocate of improved standards of care for mothers and children. The Emergency Maternity and Infant Care Program during World War II, organized and operated by Dr. Eliot, provided medical, nurs-



MARTHA M. ELIOT

ing, and hospital care for the wives and babies of men in the four lowest pay grades of the armed forces, payment for services being made by state health departments from Congressional appropriations.

DYER



R. E. DYER

The Lasker Award to Dr. Dyer honors him in several capacities: for his scientific accomplishments in the field of microbiological research, for the administration of the National Institutes of Health during the war and postwar years, and more recently, of the Research Grants Division of the Institutes Health Service. Dr. Dyer is particularly cited for expert and impartial adminis-

tration of the postwar research grants program of the Institutes which has allocated the greatest grants for medical research in world history. This program awards research fellowships, makes grants-in-aid to teaching institutions and research centers throughout the United States.

Aside from his administrative duties, which cover a period of twenty-seven years, Dr. Dyer has done considerable research on scarlet fever, typhus, Rocky Mountain spotted fever and other rickettsial diseases. In this field, he discovered that nine mile fever and "Q" fever were the same, this being one of the first steps in research on this disease. His findings that "murine typhus" could be transmitted by rat fleas to human beings, pointed the way to control of this potentially serious world public health problem.

ALDRICH

In 1944 Dr. Aldrich organized the Rochester Child Health Institute as a preventive psychiatric and well-child service for the children of the community, the first project of its kind ever undertaken. "Under his leadership, pediatricians, psychiatrists, psychologists, nursery school educators and nutritionists cooperated with city health officers, public health nurses, and the



C. ANDERSON ALDRICH

schools to discover and provide the best preventive care, physically and emotionally, for all the children of the city," according to the Lasker Award citation. The Institute was set up as a long-term project to see what could be done in a typical American community by pooling community resources for children, and developing ways of community education in physical and mental health for eventual branching out on a national scale.

HAWLEY AND MAGNUSON



PAUL R. HAWLEY

Under Dr. Hawley and Dr. Magnuson, representatives of the Lasker Group Award recipient, the Veterans Administration has six times as many full-time civilian doctors (3,659), more than fifteen times as many full-time civilian dentists (953), more than twice as many nurses (11,147), and almost seven times as many social workers (1,000) as it had in 1945.

No less than the best medical care in the world for its veterans has become a reality of the Veterans Administration Medical Division by this program.

Dr. Hawley headed the Department since August 15, 1945, as Acting Chief Medical Director on detached service from the Army. He retired in June 1946, from the Army with the rank of Major General to become Chief Medical Director for the VA. His successor, Dr. Magnuson was formerly professor of surgery and department chairman at



PAUL B. MAGNUSON

Northwestern University Medical School. In 1945, under Dr. Hawley, he perfected the residency training program of sixty-one of the country's top medical schools, and is responsible for other beneficial VA medical reorganizations. He played a major role in the affiliating for the first time of more than half of the Veterans Administration's till then isolated hospitals with Class A medical schools.

LASKER FOUNDATION



MR. AND MRS. LASKER

The Albert and Mary Lasker Foundation, donor of the awards, was established in 1943 by Mr. and Mrs. Lasker, to acknowledge work done in combating the most important causes of death and to stimulate public interest and support for this work, so that it may culminate in better health and increased life expectancy for everyone.

The Awards consist of \$1,000 each, and a gold replica of the statue, "The Winged Victory of Samothrace"—to symbolize victory over death and disease—for individual winners, and a silver statuette for Group Award winners. A leather-bound citation accompanies each Award.

The foundation presents awards in the field of planned parenthood in addition to those in medical research and public health administration.

New Drugs and Instruments

Information published in this department has been supplied by the manufacturers of the products described.

ADANON HYDROCHLORIDE

PURPOSE: Synthetic analgesic and antitussive drug.

COMPOSITION: Adanon Hydrochloride is 6-dimethylamino-4,4-diphenyl-3-heptanone hydrochloride. It is a white crystalline compound, soluble in water and alcohol, but insoluble in ether. It melts at 230-235°C., and has a bitter taste.

DESCRIPTION: In analgesic doses the action of Adanon Hydrochloride is similar in some respects to morphine. In other respects it differs from morphine, producing less stimulation and showing no tendency to the development of tolerance.

INDICATIONS FOR USE: Relief of pain from various causes, particularly intractable pain of malignancy, renal colic, and fractures. Also effective in suppressing cough, especially in pulmonary tuberculosis, if its use is guarded due to possible addiction properties. It has been ineffective in pain due to gangrene.

CAUTIONS: It is a potentially addictive drug and the same precautions must be exercised as those which surround the use of morphine.

DOSAGE AND ADMINISTRATION: May be administered orally or intramuscularly. Range of dosage by any route is from 2.5 to 10 mg. The average adult dose is 5 mg., usually increased or decreased as necessary.

HOW SUPPLIED: For oral use: Tablets of 2.5 mg., 5 mg., 7.5 mg., and 10 mg., bottles of 100 and 500. Elixir—each 5 cc. (1 teaspoonful) containing 5 mg.—bottles of 473 cc. (16 fl. oz.). For injection: Ampules of 2 cc., each 1 cc. containing 5 mg., boxes of 10, 25, and 100. Vials of 20 cc., each 1 cc. containing 10 mg.

PRODUCER: Winthrop Chemical Company, Inc., New York 13, N. Y.

TRIAZOLINE

PURPOSE: Compound sulfadiazine, sulfamerazine, and sulfathiazole.

COMPOSITION: Each Triazoline Tablet (grooved) contains 0.167 gm. of sulfadiazine, sulfamerazine, and sulfathiazole.

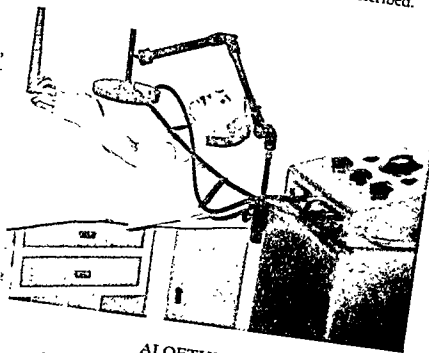
INDICATIONS FOR USE: In the treatment of any case of acute bacterial infection in which the component drugs are indicated, with the exception of meningitis.

CAUTIONS: Contraindicated in infections caused by organisms not susceptible to any of the component drugs.

DOSAGE AND ADMINISTRATION: Total dosage to be administered is the same as that which would be usual for any one of the three drugs. In adults an adequate blood level may be achieved by an initial dose of 4 to 6 gm., followed by maintenance doses of 1 gm. every four hours.

HOW SUPPLIED: Bottles of 100 and 1,000, for oral administration.

PRODUCER: Abbott Laboratories, North Chicago, Ill.



ALOETHERM

Crystal Controlled Short Wave Diathermy

DESCRIPTION: The Aloetherm operates on a frequency of 13.56 megacycles (22.12 meters), with a frequency deviation of less than 0.05 per cent. Harmonic radiation is suppressed below the 25 microvolt level required by the Federal Communications Commission.

The control panel is provided with one line switch and two control knobs, one for presetting the resonance and one for control of energy from the lowest level to the maximum output of the machine. Warm-up of the tubes is fully automatic.

The cabinet is of welded steel construction; the finish is baked, chip-proof enamel. All parts are chromium- or cadmium-plated to prevent rust. Furnished with the Inductance Cable.

PRODUCER: A. S. Aloe Company, St. Louis, Mo.

STERI-VIALS BENADRYL HYDROCHLORIDE

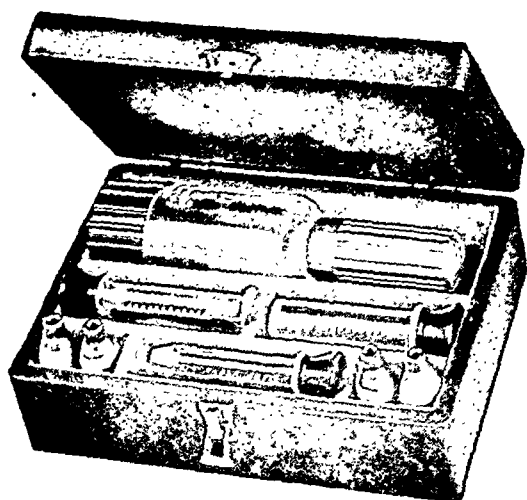
PURPOSE: For conditions in which the use of Benadryl is indicated.

DESCRIPTION: A sterile solution containing in each cc., 10 mg. of Benadryl Hydrochloride (diphenhydramine hydrochloride, P. D. & Co.).

INDICATIONS FOR USE: Indicated for acute asthma, serum reactions, bee stings, irradiation sickness, and drug reactions, particularly when the condition is urgent and immediate action of the drug is desired.

HOW SUPPLIED: In 10 cc. Steri-Vials (rubber-diaphragm-capped vials), one to a package. Benadryl also is available in 50 mg. Kapsals, bottles of 100 and 1,000; 25 mg. capsules, bottles of 100 and 1,000; and as an elixir containing 10 mg. per teaspoonful, in pint and gallon bottles.

PRODUCER: Parke, Davis & Company, Detroit 32, Mich.



KIDDE DRY ICE APPARATUS

The unit is provided with various diameter plastic applicators and solid carbon dioxide snow is formed directly into these applicators ready for immediate use and confined by the active applicator tip to the lesion itself. The low temperature of the carbon dioxide snow provides its own anesthetic.

PRODUCER: Kidde Manufacturing Co., Inc., Bloomfield, N.J.

TRI-IMMUNOL

PURPOSE: For immunizing infants and children against diphtheria, tetanus, and whooping cough with a minimum number of injections.

COMPOSITION: Tri-Immunol Trivalent Immunizing Agent is a combination of Purogenated Diphtheria Toxoid, alum precipitated, Purogenated Tetanus Toxoid, alum precipitated and Phase 1 Pertussis Vaccine.

DESCRIPTION: May be used for the "booster" injection recommended for children about to enter school. Reactions are minimal and when they do occur, they are only of local nature.

DOSAGE AND ADMINISTRATION: Should be administered in three deep intramuscular injections of 0.5 cc. each for infants and older children, with an interval of four to six weeks between injections. Immunization may be started as early as 6 months of age. The "booster" injection consists of one injection of 0.5 cc.

PRODUCER: Lederle Laboratories Division, American Cyanamid Co., Pearl River, N.Y.

PETECHIOMETER

PURPOSE: For the clinical determination of increased capillary fragility.

DESCRIPTION: The device works on the principle of negative pressure applied over the biceps. After the application of suction for a period of sixty seconds, a petechial count can be made through a magnifying lens incorporated in the head of the instrument.

PRODUCER: Rexall Drug Company, Los Angeles, Calif.

NORODIN HYDROCHLORIDE

PURPOSE: A sympathomimetic drug with psychomotor properties similar to those of amphetamine.

COMPOSITION: Norodin Hydrochloride is the Endo brand of *d*-desoxyephedrine hydrochloride (*d*-N-methyl amphetamine hydrochloride).

DESCRIPTION: Norodin acts predominantly as a central nervous system stimulant. Six milligrams produces a circulatory effect equivalent to that produced by 10 to 15 mg. of amphetamine sulfate.

INDICATIONS FOR USE: In narcolepsy, postencephalitic parkinsonism, the facilitation of roentgenographic studies of the gastrointestinal tract, and the control of appetite in obesity.

CAUTIONS: Norodin is contraindicated in hypertension, advanced arteriosclerosis, coronary artery disease, and hyperthyroidism; it should not be used in hyperexcitable or neurotic patients, or in individuals who have an idiosyncrasy to ephedrine or its analogues.

DOSAGE AND ADMINISTRATION: Since dosage varies with the individual and the condition treated, it is advisable to begin with 2.5 mg. and increase by increments of 2.5 mg. until the optimal individual dose is reached. The following total daily doses, usually given in two divided doses before noon, may be considered average:

Depressive states	2.5 mg. to 10 mg. daily
Postencephalitic parkinsonism . . .	10 mg. to 25 mg. daily
Narcolepsy	7.5 mg. to 15 mg. daily,
	divided in three equal doses

Adjunctive alcoholism treatment .	5 mg. to 10 mg. daily
Appetite inhibitor in obesity . . .	2.5 mg. to 7.5 mg. three
	times daily, thirty to
	sixty minutes before
	meals

HOW SUPPLIED: On prescription only, in 2.5 mg. tablets and 5 mg. (pink scored) tablets in bottles of 100, 500, and 1,000. It is also supplied in powder for dispensing.

PRODUCER: Endo Products, Inc., Richmond Hill 18, N.Y.

CRESATIN OINTMENT

PURPOSE: Fungicide for treatment of mycotic skin infections. COMPOSITION: Contains 80 per cent metacresylacetate in an especially prepared ethyl cellulose base.

INDICATIONS FOR USE: In the treatment of common mycotic skin infections such as tinea circinata, tinea versicolor, tinea cruris, erythrasma and dermatophytosis or ringworm of the feet.

HOW SUPPLIED: In 1/4 ounce collapsible tubes.

PRODUCER: Sharp & Dohme, Inc., Philadelphia 1, Pa.

AMPINS

PURPOSE: For administering emergency drugs, such as morphine, epinephrine, nikethamide, etc.

DESCRIPTION: The material to be injected is sealed into the special drawn ampule under pressure, using an inert gas. When the Ampin is held in a pencil position (bottom up), and the tip of the ampule broken, the inert gas forces the medication through the needle into the tissue. Just enough pressure is used to accomplish this result. The entire unit is sterilized after assembly.

HOW SUPPLIED: In packages of 5 Ampins.

PRODUCER: Strong Cobb & Co., Inc., Cleveland 4, O.

STERILE AQUEOUS SUSPENSION ESTROGENIC SUBSTANCES, R & C

PURPOSE: Estrogenic therapy.

COMPOSITION: The preparation contains biologically standardized natural estrogens (90 per cent or more estrone).

INDICATIONS FOR USE: For intramuscular injection where prolonged estrogenic activity is desired, as in the treatment of the menopausal syndrome.

CAUTIONS: Contraindicated in the treatment of women who have a familial or personal history of mammary or genital malignancy.

DOSE AND ADMINISTRATION: Usually 1 cc. (20,000 I.U.) injected intramuscularly once or twice weekly as required. Before withdrawal of the suspension, the vial should be shaken gently, or the contents agitated with a rolling motion to insure even dispersion.

HOW SUPPLIED: Multidose 5 cc. and 10 cc. vials, assayed biologically so that each cc. when uniformly suspended contains the equivalent of 20,000 I.U. standard estrone.

PRODUCER: Reed & Carnrick, Jersey City, N.J.

GLYTHEONATE

COMPOSITION: Each tablet contains Theophylline sodium glycinate 5 gr. (324 mg.), equivalent to theophylline U.S.P. 2½ gr. (162 mg.); phenobarbital ¼ gr. (16.2 mg.); ractephrine hydrochloride ¼ gr. (24.3 mg.).

INDICATIONS FOR USE: In respiratory involvements such as asthma and hay fever, either allergic or secondary to bronchitis or emphysema.

CAUTIONS: Due to the ractephrine content, use cautiously in hypertension and cardiorenal disease, diabetes, and hyperthyroidism.

DOSE: Clinical data suggest an average therapeutic dose of 1 to 2 tablets three times a day.

HOW SUPPLIED: Bottles of 100 tablets.

PRODUCER: The E. L. Patch Company, Boston, Mass.

ELAMINE LYOPHILIZED

PURPOSE: Parenteral amino acid therapy.

COMPOSITION: Free amino acids (96 per cent), of which more than 50 per cent are amino acids essential for nitrogen balance in man.

DESCRIPTION: A modified acid hydrolysate of casein, to which tryptophane is added and from which glutamic and aspartic acids have been partially removed. The pH ranges from 6.5 to 7.0. The total nitrogen is 13.4 per cent, of which 75 per cent is represented by α-amino nitrogen. The product is sterile, nonpyrogenic, and nonantigenic.

DOSE AND ADMINISTRATION: 60 gm. of Elamine Lyophilized will keep the average surgical patient in nitrogen equilibrium. In severe cases of protein deficiency, from 2 to 4 times this dose may be given without creating untoward effects. The product may be restored to solution with any U.S.P. parenteral diluent—water for injection, dextrose solution, normal saline. It is given as a 10 per cent solution at a rate of 50 to 100 drops per minute.

HOW SUPPLIED: 12x60 gm. per bottle in a shipping carton or 6x60 gm. per bottle plus 6 bottles of diluent and 6 infusion kits.

PRODUCER: Interchemical Corporation, Biochemical Division, Union, N.J.

PRESIDON

PURPOSE: Sedative-hypnotic.

COMPOSITION: Presidon is a pyridine derivative, and is not a barbiturate.

INDICATIONS FOR USE: Especially useful for broken sleep, premature awakening, as a daytime sedative and for ambulatory cases of insomnia. With therapeutic doses, there is little likelihood of "hangover," side reactions, or cumulative effects.

HOW SUPPLIED: In scored 0.2 gm. tablets, bottles of 20 and 100.

PRODUCER: Hoffman-La Roche, Inc., Nutley, N.J.

BENZEBAR

PURPOSE: A combination of benzedrine sulfate and phenobarbital for treatment of depressive states.

COMPOSITION: Each tablet contains: Benzedrine sulfate (racemic amphetamine sulfate, S.K.F.), 5 mg. (1/13 gr.); and phenobarbital, ¼ gr. (16 mg.).

INDICATIONS FOR USE: In depressive states, particularly those following: onset of menopause, acute infectious diseases, surgical operations, childbirth; or associated with: chronic organic disease, persistent pain, old age, grief over misfortune or bereavement. These states are often accompanied by debilitating anxiety, apprehension, agitation, or nervousness.

CAUTIONS: Should not be used in patients hypersensitive to ephedrine-like compounds, or in cases of coronary disease or other cardiac conditions in which vasoconstrictors are contraindicated. Should be used with caution in the presence of hypertension.

DOSE AND ADMINISTRATION: Suggested dosage is 2 to 4 tablets daily, one-half the dosage on arising, and the other half before noon.

HOW SUPPLIED: In bottles of 25 tablets.

PRODUCER: Smith, Kline & French Laboratories, Philadelphia, Pa.

DIENESTROL SUSPENSION

PURPOSE: For treatment of menopausal symptoms, prevention of breast engorgement and suppression of lactation.

DESCRIPTION: Unlike oil solutions, the aqueous medium is readily absorbed without foreign body reactions or local irritation.

COMPOSITION: A sterile solution containing microcrystals of Dienestrol, ranging from 3 to 5 microns in diameter, in normal saline, with 0.5 per cent chlorobutanol as bacteriostatic agent.

DOSE AND ADMINISTRATION: For intramuscular injection. A 1½ inch, 23 gauge needle is recommended. When vial is thoroughly shaken, each cc. contains 5 mg. of Dienestrol. Menopausal symptoms: 2.5 to 5 mg. (½ to 1 cc.), injected in the deltoid or gluteal muscle, once or twice weekly. For inhibition of breast engorgement or suppression of lactation: 5 to 10 mg. (1 to 2 cc.), administered intramuscularly for three to four days.

HOW SUPPLIED: In 10 cc. multiple dose, rubber-stoppered vials, each cc. contains 5 mg. Dienestrol.

PRODUCER: White Laboratories, Inc., Newark, N.J.

POSTGRADUATE COURSES

Complete information may be obtained by writing directly to the Institutions offering the courses.

Selected Postgraduate Continuation Courses for Practicing Physicians—Beginning January 1, 1949.

ALLERGY

<i>Institution</i>	<i>Title of Course</i>	<i>Schedule of Course</i>	<i>Registration Fee and/or Tuition</i>
New York Postgraduate Medical School, New York	#302—Allergy	Part time, Fridays, Jan. 7-Feb. 25, 1949	\$ 25.00

ANESTHESIOLOGY

Cook County Graduate School of Medicine, Chicago	Personal Course in Ether and Nitrous Oxide (Inhalation) Anesthesia	1 month, full time, every month	125.00
	Personal Course in Ether, Nitrous Oxide, Ethylene, and Cyclopropane (Inhalation) Anesthesia	1 month, full time, every month	200.00
	Personal Course in Spinal and Intravenous Anesthesia	2 weeks, full time, every two weeks	150.00
	Two Week Personal Course in Endotracheal Anesthesia	2 weeks, full time, every two weeks	150.00
New York Postgraduate Medical School, New York	#942—Anesthesia (Specialists)	2 weeks, full time, third week	125.00 65.00 (Specialists)

ARTHRITIS

New York Postgraduate Medical School, New York	#301—Arthritis and Allied Rheumatic Disorders	Tuesdays, part time, Jan. 4-Feb. 15, 1949	45.00
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CARDIOVASCULAR DISEASES

New York Medical College, Flower and Fifth Avenue Hospitals, New York	Cardiology	20 successive Wednesdays, may begin any Wednesday except during July and Aug.	150.00
New York Postgraduate Medical School, New York	#303—Clinical Cardiology	Jan. 3-Feb. 21, 1949, part time	45.00
Graduate School of Medicine, University of Pennsylvania, Philadelphia and Philadelphia General Hospital	Cardiology	8 Thursdays, Jan., 1949	80.00

CHEST DISEASES

New York Postgraduate Medical School, New York	#308—Acute and Chronic Diseases of the Chest	Thursdays, part time, Jan. 6-Feb. 24, 1949	45.00
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DERMATOLOGY AND SYPHILOLOGY

Cook County Graduate School of Medicine, Chicago	Clinical Dermatology	2 weeks, full time, every 2 weeks	75.00
New York Polyclinic Medical School and Hospital, New York	Dermatology and Syphilology	6 weeks, part time, first of any month	100.00
	Dermatology and Syphilology	3 months, part time, first of any month	200.00

DIABETES

New York Postgraduate Medical School, New York	#313—Diabetes Mellitus, Nephritis and Hypertension	Thursdays, part time, Jan. 6-Feb. 24, 1949	45.00
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POSTGRADUATE COURSES

Selected Postgraduate Continuation Courses for Practicing Physicians—Beginning January 1, 1949.

ELECTROCARDIOGRAPHY

<i>Institution</i>	<i>Title of Course</i>	<i>Schedule of Course</i>	<i>Registration Fee and/or Tuition</i>
University Extension, University of California Medical School, Los Angeles, in cooperation with University Medical Extension, University of California, San Francisco At: University Extension, Los Angeles	Electrocardiography	3 weeks, part time, Jan. 5-20, 1949	\$ 25.00

ENDOCRINOLOGY

New York Postgraduate Medical School, New York	# 222—Gynecological Endocrinology	24 sessions, part time, beginning Jan. 4, 1949	150.00
	# 309—Diseases of the Thyroid and Other Endocrine Glands and Disorders of Nutrition	Fridays, part time, Jan. 7-Feb. 25, 1949	45.00

ENDOSCOPY

Cook County Graduate School of Medicine, Chicago	Practical Cystoscopy	10 days, part time, every two weeks	150.00
New York Postgraduate Medical School, New York	# 211—Cystoscopy and Endoscopy	15 sessions, part time, beginning Jan. 3, 1949	75.00

GASTROENTEROLOGY

New York Polyclinic Medical School and Hospital, New York	Gastroenterology	6 weeks, part time, beginning Jan. 2, 1949	50.00
	Gastroenterology	3 months, part time, beginning Jan. 2, 1949	75.00
	Proctology, Gastroenterology, Operative Proctology (Cadaver)	6 weeks, part time, beginning Jan. 2, 1949	200.00
New York Postgraduate Medical School, New York	# 311—Gastroenterology	7 weeks, part time, Jan. 5-Feb. 23, 1949	45.00

HEMATOLOGY

Graduate Division of the School of Medicine, University of Southern California, Los Angeles At: Los Angeles County Hospital	Course No. 738—Hematology	12 weeks, part time, beginning Jan. 3, 1949	50.00
	# 306—Clinical Hematology	Wednesdays, part time, Jan. 5-Feb. 23, 1949	30.00
New York Postgraduate Medical School, New York			

INTERNAL MEDICINE

Graduate Division of the School of Medicine, University of Southern California, Los Angeles At: Los Angeles County Hospital	Clinical Review of Internal Medicine (Course No. 730)	12 weeks, full time, Jan. 3, 1949	250.00
	Internal Medicine (Course No. 731)	9 months, full time, Jan., 1949	750.00
Tufts College Medical School, Postgraduate Division, Boston At: Pratt Diagnostic Hospital	Internal Medicine (as related to Basic Sciences)	8 weeks, Jan. 3-Feb. 26, 1949	200.00 Tuition 5.00 Reg. Fee

POSTGRADUATE COURSES

Selected Postgraduate Continuation Courses for Practicing Physicians—Beginning January 1, 1949.

<i>Institution</i>	<i>Title of Course</i>	<i>Schedule of Course</i>	<i>Registration Fee and/or Tuition</i>
New York Postgraduate Medical School, New York	#300—Seminar in Internal Medicine	8 weeks, full time, Jan. 3-Feb. 25, 1949	\$300.00
	#307—Problems in Diagnosis (Internal Medicine)	Mondays, part time, Jan. 3-Feb. 21, 1949	45.00
	#310—Diseases of the Liver and Biliary Tract	Wednesdays, part time, Jan. 5-Feb. 23, 1949	30.00
	#315—Psychological Aspects of Internal Medicine	Fridays, part time, Jan. 7-Feb. 25, 1949	25.00
	#319—Peripheral Vascular Diseases	Tuesdays, part time, Jan. 4-Feb. 15, 1949	30.00

MEDICINE, GENERAL

Mey Clinic, Boston At: Clinic Auditorium	Medical Clinics	Tuesdays and Thursdays throughout the entire year	Not given
	Two-Hour Clinical Symposium on General Clinical Subjects	Wednesday nights, throughout the year, beginning Oct. 1, 1948	Not given
New York Polyclinic Medical School and Hospital, New York	Course for General Practitioners	6 weeks, full time, beginning Jan. 2, 1949	100.00
	Course for General Practitioners	3 months, full time, beginning Jan. 2, 1949	200.00

NEUROLOGY AND PSYCHIATRY

Graduate Division of the School of Medicine, University of Southern California, Los Angeles At: Los Angeles County Hospital	Course No. 742—Psychosomatic Medicine	12 weeks, part time, beginning Jan. 5, 1949	50.00
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NUTRITION

New York Postgraduate Medical School, New York	#309—Diseases of the Thyroid and Other Endocrine Glands and Disorders of Nutrition	Fridays, part time, Jan. 7-Feb. 25, 1949	45.00
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OBSTETRICS AND GYNECOLOGY

New York Postgraduate Medical School, New York	#200—Seminar in Gynecology	2 months, full time, beginning Jan. 3, 1949	300.00
	#203—Diagnosis and Office Treatment (Gynecology)	15 sessions, part time, beginning Jan. 3, 1949	75.00
	#223—Vaginal Cytology (Specialists)	8 weeks, part time, beginning Jan. 4, 1949	100.00
University of Oklahoma School of Medicine and University Hospitals, Oklahoma City At: State Medical School of Oklahoma, Oklahoma City	Postgraduate Course in Pediatrics and Postgraduate Course in Obstetrics	5 days, quarterly	None

OPHTHALMOLOGY

Graduate School of Medicine, University of Florida, Jacksonville At: Miami Beach, Florida	Midwinter Seminar in Otolaryngology and Ophthalmology	6 days, full time, Jan. 10-15, 1949	Not given
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POSTGRADUATE COURSES

Selected Postgraduate Continuation Courses for Practicing Physicians—Beginning January 1, 1949.

<i>Institution</i>	<i>Title of Course</i>	<i>Schedule of Course</i>	<i>Registration Fee and/or Tuition</i>
Harvard Medical School, Courses for Graduates, Boston	Clinical Ophthalmology	1 month, full time, Jan. 3-29, 1949	\$150.00
At: Harvard Medical School and Massachusetts Eye and Ear Infirmary			75.00 Tuition
Tufts College Medical School, Postgraduate Division, Boston	Ophthalmoscopy	1 month, part time, Jan. 10-Feb. 4, 1949	5.00 Reg. Fee
At: Boston Dispensary	Clinical Otolaryngology and Ophthalmology	6 weeks, full time, Jan. 2, 1949	100.00
New York Polyclinic Medical School and Hospital, New York	Clinical Otolaryngology and Ophthalmology	3 months, full time, Jan. 2, 1949	
	Ophthalmology	6 weeks, part time, Jan. 2, 1949	150.00
	Ophthalmology	3 months, part time, Jan. 2, 1949	50.00
	Ophthalmology, Including Operative Ophthalmology (Cadaver) and Refraction	3 months, part time, Jan. 2, 1949	75.00
			275.00
	Ophthalmology and Otolaryngology, Including Cadaver Courses and Refraction	3 months, full time, Jan. 2, 1949	600.00

ORTHOPEDIC SURGERY

New York Postgraduate Medical School, New York	#500—Seminar in Orthopedic Surgery (Specialists)	10 days, full time, Jan. 3-14, 1949	125.00
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OTOLARYNGOLOGY

Graduate School of Medicine, University of Florida, Jacksonville At: Miami Beach, Florida	Midwinter Seminar in Otolaryngology and Ophthalmology	6 days, full time, Jan. 10-15, 1949	Not given
New York Polyclinic Medical School and Hospital, New York	Clinical Otolaryngology	6 weeks, part time, Jan. 2, 1949	75.00
	Clinical Otolaryngology	3 months, part time, Jan. 2, 1949	100.00
	Clinical Otolaryngology and Ophthalmology	6 weeks, full time, Jan. 2, 1949	100.00
	Clinical Otolaryngology and Ophthalmology	3 months, full time, Jan. 2, 1949	150.00
	Ophthalmology and Otolaryngology Including Cadaver Courses and Refraction	3 months, full time, Jan. 2, 1949	600.00

PATHOLOGY

Cook County Graduate School of Medicine, Chicago	Gross Pathology	1 month, full time, every month	150.00
	One Month Course—Surgical Pathology	4 weeks, full time, every month	250.00
	Two Weeks Course in Surgical Pathology	2 weeks, full time, every two weeks	150.00

POSTGRADUATE COURSES

Selected Postgraduate Continuation Courses for Practicing Physicians—Beginning January 1, 1949.

PEDIATRICS

<i>Institution</i>	<i>Title of Course</i>	<i>Schedule of Course</i>	<i>Registration Fee and/or Tuition</i>
Harvard Medical School, Courses for Graduates, Boston At: Children's Hospital	Pediatrics	4 months, full time, Jan. 3-Apr. 28, 1949	\$500.00
New York Medical College, Flower and Fifth Avenue Hospitals, New York	Clinical Pediatrics	1 month, all year, full time	150.00
	Clinical Pediatrics	3 months, all year, full time	250.00
New York Postgraduate Medical School, New York	#410—Clinical Pediatrics	4 weeks, full time, Jan. 3-29, 1949	150.00

POLIOMYELITIS

Georgia Warm Springs Foundation, Warm Springs	Care of Acute and Convalescent Poliomyelitis	1 week, Jan. 3, 1949	None
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PROCTOLOGY

Tufts College Medical School, Postgraduate Division, Boston At: Boston Dispensary and Associated Clinics	Proctology III (Proctology I is prerequisite to Proctology III)	1 month, part time, Jan. 3-29, 1949. (Course may be taken 6 days a week for one month or 3 days a week for 2 months)	100.00 Tuition 5.00 Reg. Fee
New York Polyclinic Medical School and Hospital, New York	Proctology	6 weeks, part time, Jan. 2, 1949	75.00
	Proctology, Gastroenterology, Operative Proctology (Cadaver)	6 weeks, part time, Jan. 2, 1949	200.00

PUBLIC HEALTH

Ohio State Department of Health, Columbus At: Oberlin, Ohio	Field Training, Orientation and Public Health Administration	1 month, special arrangement	None
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RADIOLOGY

Cook County Graduate School of Medicine, Chicago	Clinical Roentgenology	2 weeks, full time, 3rd Monday of each month	70.00
	#1—Diagnostic Roentgenology	2 weeks, full time, 1st Monday of each month	125.00
	One Month Course—Clinical Roentgenology	4 weeks, full time, 3rd Monday of each month	125.00
	Radiation Therapy	2 weeks, full time, every two weeks	110.00
	Radiation Therapy	4 weeks, full time, every month	200.00
	Radiation Therapy	2 months, full time, every month	300.00
Harvard Medical School, Courses for Graduates, Boston At: Children's Hospital	Pediatric Radiology (limited to physicians who have a working knowledge of Radiology)	1 month, full time, monthly	150.00
At: Massachusetts General Hospital	General Radiology (limited to physicians who have a working knowledge of Radiology)	1 month, full time, monthly	150.00

POSTGRADUATE COURSES

Selected Postgraduate Continuation Courses for Practicing Physicians—Beginning January 1, 1949.

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
At: Peter Bent Brigham Hospital	General Radiology (limited to physicians who have a working knowledge of Radiology)	1 month, full time, monthly	\$150.00
New York Medical College, Flower and Fifth Avenue Hospitals, New York	Diagnostic Roentgenology	6 weeks, half time, every 6 weeks except during July and Aug.	150.00
New York Polyclinic Medical School and Hospital, New York	Radiology	3 months, full time, Jan. 2, 1949	300.00
SURGERY			
New York Polyclinic Medical School and Hospital, New York	Clinical Surgery	6 weeks, full time, Jan. 2, 1949	100.00
	Combined Surgical Course Including Cadaver Surgery and Gynecology	3 months, full time, Jan. 2, 1949	350.00
THERAPY			
Cook County Graduate School of Medicine, Chicago	Radiation Therapy	2 weeks, full time, every two weeks	110.00
	Radiation Therapy	4 weeks, full time, every month	200.00
	Radiation Therapy	2 months, full time, every month	300.00
UROLOGY			
New York Hospital (James Buchanan Brady Foundation), New York	Postgraduate Course in Urology	31 weeks, full time, 6 months or longer, Jan. 1, 1949 (31 weeks, full time, for veterans; 6 months or longer for others)	500.00
New York Postgraduate Medical School, New York	#1010—Advanced Course in Urology for Specialists	2 months, full time, Jan. 3-Feb. 26, 1949	300.00

ADDRESSES OF SCHOOLS LISTED

CALIFORNIA
Graduate Division of the School of Medicine, University of Southern California, Los Angeles 7, California.
University Extension, University of California Medical School, Los Angeles 24, California.
University Medical Extension, University of California, San Francisco 22, California.

FLORIDA
University of Florida Graduate School of Medicine, 2033 Riverside Avenue, Jacksonville, Florida.

GEORGIA
Georgia Warm Springs Foundation, Warm Springs, Georgia.

ILLINOIS
Cook County Graduate School of Medicine, 427 South Honore Street, Chicago 12, Illinois.

MASSACHUSETTS
Harvard Medical School, Courses for Graduates, 25 Shattuck Street, Boston 15, Massachusetts.
Lahey Clinic, 605 Commonwealth Avenue, Boston 15, Massachusetts.

Tufts College Medical School, Postgraduate Division, 30 Bennett Street, Boston 11, Massachusetts.

NEW YORK
New York Hospital (James Buchanan Brady Foundation), 525 East 68th Street, New York 21, New York.
New York Medical College, Flower and Fifth Avenue Hospitals, 20 East 106th Street, New York 29, New York.
New York Polyclinic Medical School and Hospital, 345 West 50th Street, New York 19, New York.
New York Postgraduate Medical School, 303 East 20th Street, New York 3, New York.

OKLAHOMA
University of Oklahoma School of Medicine and University Hospitals, 800 Northeast 13th Street, Oklahoma City 4, Oklahoma.

OHIO
Ohio State Department of Health, 306 Ohio Depts. Building, Columbus 15, Ohio.

PENNSYLVANIA
University of Pennsylvania Graduate School of Medicine, 237 Medical Laboratories, Philadelphia 4, Pennsylvania.

Leaves from a Doctor's Diary

By MAURICE CHIDECKEL

November 1 . . . Man's pretense to be a reasoning animal is a misrepresentation at times, a forgery, a lie, if you please. Apropos of the case of intestinal amebiasis, treated with emetine by capable Dr. Gibbons. The patient died of a severe myocarditis. I don't know whether liver involvement is or is not present in such cases. Nor do I know whether it was the toxicity of the emetine that killed the patient. Perhaps it were better to have used a non-toxic drug, say, chloroquine, instead of emetine.

But was it sensible, was it ethical on the part of Dr. John O'Higgins to tell a neighbor of the dead man that it was bad treatment that killed the patient? The two bully brothers of the deceased threatened to make mincemeat out of Dr. Gibbons. And Dr. O'Higgins is a dignified, sensible looking gentleman.

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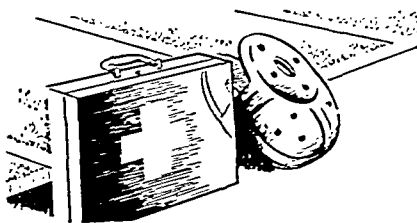
November 2 . . . Boldly planned and triumphantly achieved by refugee Dr. Kaltenheimer, Mrs. Snellenburger, also a refugee, simply had to have a baby, or her Americanized husband threatened to leave her in the cold. The husband's sperm, to use the expression of Dr. Kaltenheimer, "is very dead." Sly Dr. Colton suggested artificial insemination. "Goot, so goot," joyously exclaimed the imported medico. It was done unbeknown to hubby. And the lady conceived, and she was with child and gave birth to it—a boy.

How adoringly "papa" gazed at his "offspring." And he spoke. "Did you ever, ever, see such a striking resemblance of father to son?—Just me in miniature." Dr. Colton pressed the poor refugee physician for details. Where did he get the donor? How much was he paid? Kaltenheimer shrugged his shoulders. This, and nothing else.

Then Dr. Colton passed judgment: "It was not artificial insemination." Oh, well, could be.

* * *

November 6 . . . Colleague Slade and I walked around the clinic and discussed the cases of two young men, two tragedies. One underwent a thorough physical in the morning for a football team, and was declared a fine specimen. After half an hour of strenuous exercise he dropped dead. Death for this boy of 24 proved to be due to atherosclerosis of both coronaries.



The other case was that of a young man who underwent a premarital examination and was given a clean bill of health. He went on his honeymoon and after coitus with the bride his headache became so violent that he was brought home where he died. Death was due to intracranial hemorrhage, caused by a tiny aneurysm in the circle of Willis. "There is your value of our physical," gloomily spoke my companion.

A soft hand was laid on his shoulder, the one belonging to Mrs. Paperman. "Just coming from your office. You must tell me what to do. My husband keeps on talking in his sleep a whole night, and I can't close my eyes. What am I to do?" Angrily Dr. Slade answered: "Give him a chance to say a few words during the day and he'll keep quiet during the night." Said she: "Will that really help? Oh, thank you."

November 10 . . . Says Dr. Random to me: "Have you seen that rare case of complete atresia of the esophagus with the lower end communicating with the trachea near the bifurcation? Did you notice the upper segment ending in a blind pouch? Well, I am to ligate the fistula. I'll try to collect the fee in advance. Why? Well, he may not survive the ligation. He. . ." His wife approached him. "Nice girl, if she would not be so talkative. Talks and talks and says absolutely nothing." "Oh, darling," she began, "I was over at the fashion show. It's sublime, wonderful. It absolutely made me speechless." From him: "Well, if it made you speechless, I'll buy the whole outfit, regardless of price. Wonderful investment." Her eyes spat fire. "Brute," she screamed, "I never want to see you again," and away she rushed. He smiled. "She'll come back. Anything to make her speechless, if only for a week, is worth the price."

* * *

November 12 . . . Told John Fairchild, 88, that he was suffering from pulmonary tuberculosis in advanced stage. One more proof of the laity's misconception that it never occurs in the aged. The old gentleman fell to thinking. "So I can't get married. Or can I? Bad. She'll be disappointed. Planned a honeymoon. Sorry I came here."

Not Mrs. Pratt, whose husband, 79, suffers from thromboembolism. I warned her that the elderly man must stay out of bed in order to avoid a lethal catastrophe. I explained to her the danger of the absence of leg movement and the obstruction to the blood flow by flexion of the thighs. "Gosh," she addressed herself to her woman companion in the hall, "I am glad I came here. I thought he must stay in bed, so I made him walk. Now, to bed he goes. What do you think of that dope, the doctor? Does he think I married that antique for love?" Said the companion: "Dope is right."

LEAVES FROM A DOCTOR'S DIARY

November 15 . . . Dr. Lewis Elmer's life is devoted to the exploration of the abnormal mind. He can interpret the fears, the resolves, the deceptions, the laughter, the fury of the insane. The vague, the furiously unbalanced, he can translate and form into impressions. As an experiment, he tried to persecute one inmate of a mental hospital. That inmate loved and adored Dr. Elmer. This, he explained to me, is the affinity between the hunter and the hunted.

The doctor began to devote a great deal of his time to that inmate of 21, who was illegitimate and the son of a prostitute. He came to the conclusion that the boy was never insane, only a lonely, misguided child who had fallen in bad company. Himself childless, the doctor adopted him, took him to his house, educated him. It was a happy family circle, for the former inmate was very ingratiating and one can say charming. And suddenly, because of an imaginary affront, he turned against his benefactor. Dr. Elmer is in the hospital with four broken ribs and a fractured lower maxilla. Back in the asylum his mate has only one wish: Finish his job. "Who did he think I was? A lunatic?" Unable to speak, Dr. Elmer wrote on a paper: "You cannot universalize the abnormal."

The normal, as said Jacobi long ago, is a myth. Patient Ludwig demanded that I give him back the medical fee he paid me after an examination, because he decided not to take the prescription. Is he normal? And when I granted his request, am I normal?

November 18 . . . There he stood, Claude Whitaker, in a dress shop. It was a stormy discussion, because of his case. Rhetorical Lucille, our feminine cardiologist wrote these words in her report: "He attracted the first bolts of lightning from the storm clouds of progressive medicine."

Claude's was an everyday case of coronary thrombosis. As his coronary time was found normal, he was to be given dicumarol and heparin. Dr. Robert forcibly took away the medication from the hands of the interne. He proclaimed what we already heard and knew, that in the episodes of coronary occlusion, there is rather a tendency to bleeding into the wall of the artery, which causes the thrombosis. Hence instead of an anticoagulant, we must administer a drug that will promote coagulation. Claude Whitaker was given dicumarol and there he was. Orthopedic surgeon G. and I wanted to go in and talk about his condition. But he had a customer, one of those females that look blissfully ignorant and incurably vain. We saw him take out one dress after another, and we decided to stop in on our way back.



More than an hour later, the same customer was still there. The store looked like the aftermath of a Russian pogrom and Claude was on the point of collapse. The counters were piled up with dresses, all boxes empty, with the exception of one on the shelf. "Well," she finally said, "I really didn't come to buy anything. I had a couple of hours to spend, so I thought I'd look at some dresses. You don't mind, do you?" Dr. G. suggested that I break her nose and then take her to his office and he'd set it. Claude was still smiling. "In this case, lady, will you still permit me to show you the last dress we have here. Only the one left that you haven't seen." He benevolently condescended. Believe it or not, that dress she bought, actually paid for, and left with it.

November 22 . . . Some insignificant.

Two middle-aged women left the clinic angrily, when the examiner insisted that they state their correct age. So said Anatole France once, "I'd rather ask an old man when he expected to die than an old woman when she was born."



An old man laughed hilariously when Dr. Gallagher told him to stop drinking twelve cups of coffee a day, because coffee is a slow poison. "Very, very slow," he spoke aloud. "Been drinking it for sixty-eight years."

Because of the tannin in tea which may be a cause of constipation, Russian born Fyodor Malinov was asked how much tea he drank in a day. Answer: Twenty-two saucers.

Samuel Gellerman is in a hospital with a burned face, because of lye thrown at him by his sweetheart, when she learned of a date he had with another young woman. So said William Congreve:

Heaven has no rage like love to hatred turned,
Nor Hell a fury like a woman scorned.

Pious Sol Roberts with youth far behind him, met beautiful Mathilde in my waiting room. He offered his life for one kiss from her and she refused to sell her kisses so cheap.

And from all the men and women I meet and treat, I have learned that man's mind is the most unexplored region, and will remain unexplored until the end of time, for there is no such thing as the embodiment of intellect. The man, even the learned man, who believes in the self sufficiency of his own thought is deceiving himself. The man with a complete mind is as yet unborn, and never will be.

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